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PSYCHOPHARMACOLOGY IN AVIATION AND ASTRONAUTICS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 3-11

[Article by P. V. Vasil'yev and G. D. Glod, submitted 20 Jul 76]

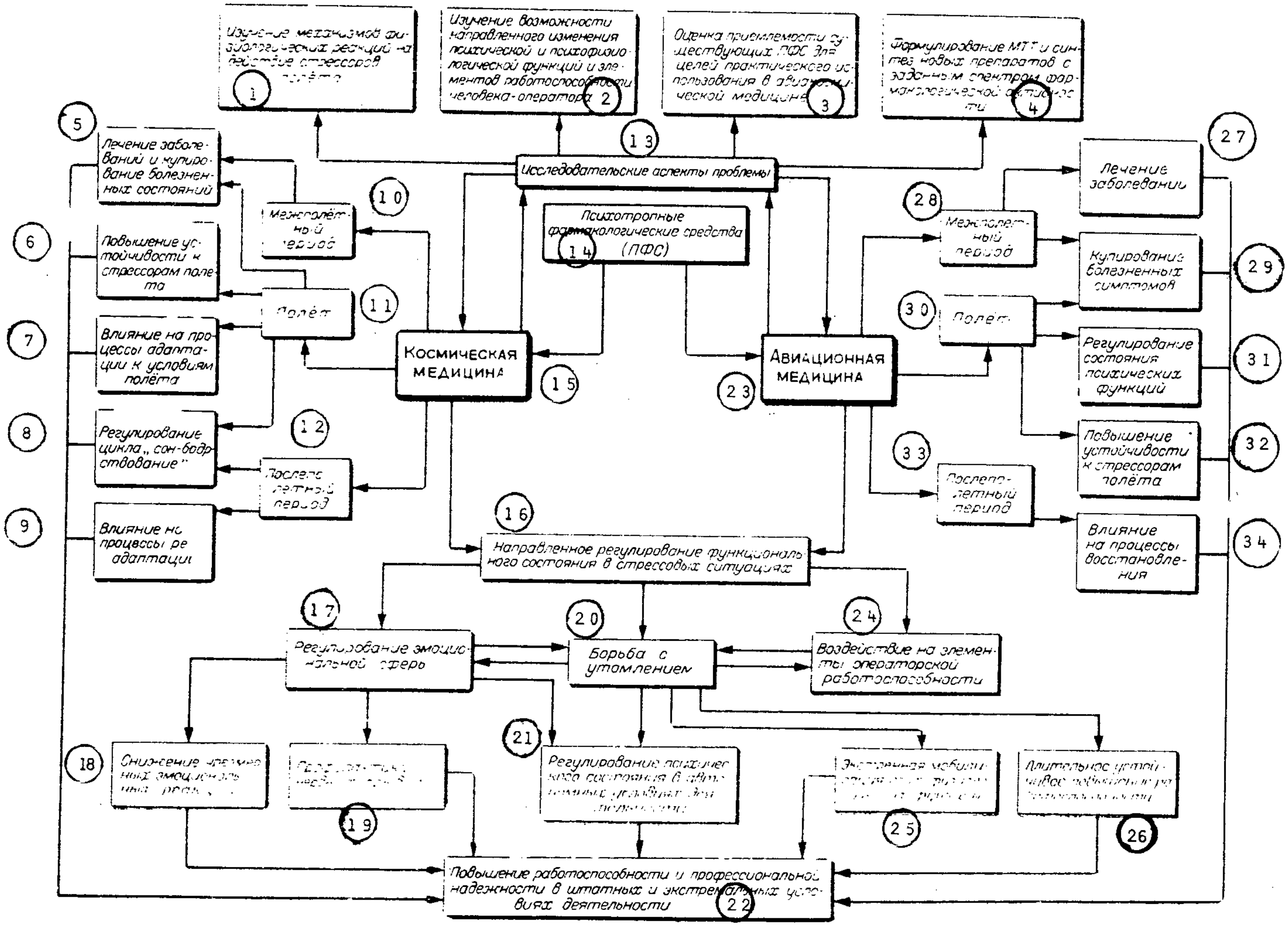
[Text] The refinement of aerospace technology has a substantial effect on the nature of professional activity of crews, making it increasingly tense and responsible. As a result there may be stress and depletion of compensatory reactions and, as a consequence, diminished efficiency of crew members involved in regular and particularly unforeseen flying conditions.

The foregoing convinces us of the urgency of searching for new ways and means of maintaining a high degree of efficiency and professional reliability of crews.

In this regard, pharmacological agents with psychotropic action are of some promise. The theoretical and applied aspects of using psychopharmacological agents (PPA) in aerospace medicine are quite diverse (see Chart).

Each of them merits special consideration. However, the pathogenesis of impaired efficiency of pilots and astronauts in flight and the capabilities of current PPA give us grounds to consider two main directions of application of PPA to be the most promising at the present time: for the prevention or correction of functional disturbances in the central nervous system that are related to fatigue, and for controlled regulation of emotions.

The use of PPA as levers to control the functional state of the organism increases efficiency and professional reliability of the [human] operator under standard and particularly extreme operating conditions. The following special problems are being resolved on the way toward this ultimate goal: reduction of signs of fatigue and maintenance of a high degree of efficiency; emergency mobilization of psychophysiological functions when necessary; prolonged and stable increase of efficency; regulation of processes of adaptation to new and unusual conditions; curbing excessive emotional reactions; prevention of stress and nervous breakdown; increasing resistance of the organism to some deleterious factors, etc.



Basic chart of probable directions of use of PPA in aerospace medicine
[See key on the following page]

Key to Chart:

1) investigation of mechanisms of physiological reactions to stressors related to flight
2) investigation of possibility of controlled alteration of mental and psychophysiological functions and elements of operator efficiency
3) evaluation of suitability of existing PPA for practical use in aerospace medicine
4) formulation of medicotechnical requirements and synthesis of new products with assigned spectrum of pharmacological activity
5) treatment of disease and arrest of morbid states
6) increasing resistance to flight stressors
7) affecting processes of adaptation to flight conditions
8) regulation of "sleep--waking" cycle
9) influencing readaptation processes
10) interflight period
11) flight
12) postflight period
13) research aspects of the problem
14) psychotrophic pharmacological agents (PPA)
15) space medicine
16) controlled regulation of functional states in stress situations
17) regulation of emotions
18) lowering excessive emotional reactions
19) prevention of nervous breakdowns
20) control of fatigue
21) regulation of mental states under autonomic performance conditions
22) raising efficiency and professional reliability under standard and extreme condittions
23) aviation medicine
24) influencing elements of operator efficiency
25) emergency [immediate] mobilization of psychophysiological functions
26) prolonged and stable increase of efficiency
27) treatment of diseases
28) interflight period
29) curbing morbid symptoms
30) flight
31) regulation of state of mental functions
32) increasing resistance to flight stressors
33) postflight period
34) influencing recovery processes

There is a history to the control of fatigue by means of PPA with psychostimulating action. Man's first attempts to artificially increase his efficiency go back to antiquity. In ancient Rome, the stimulant beverage, hydromel, was used [93]. Philostratus and Galen reported that athletes took stimulants at Olympic games to improve their athletic achievements [63]. In Russia, such medicinal plants as the tea plant [Lycium barbarum L.], "levzeya" [probably snapdragon family] and lemon tree [could be Schizandra also] were used since olden times [45]. In the years of the Great Patriotic War, phenylalkylamines and cola products were used in the armies of belligerent countries, including our air corps [10, 23, 27, 47, 48, 50-53, and others]. The cited authors reported that the psychostimulants were rather effective, but indicated that efforts to mobilize psychophysiological functions immediately and appreciably were limited in many respects by the side-effects of phenamine and rather frequent instances (up to 15%) of paradoxical reactions to the drug.

In postwar years, there was significant decrease in interest of researchers in the problem of psychostimulants. Nor was it developed and applied in the field of athletics, because of the negative attitude toward drug addiction ["doping"]. It is only in the last few decades, against the background of increased interest in problems of psychopharmacological regulation of functional state of the organism that a series of works was published, dealing with research and comprehensive clinicopharmacological investigation of new representatives in this group of products. Thanks to the research of I. I. Brekhman, A. S. Saratikov, A. D. Turova and a number of other authors, a new group of stimulants of plant origin was adopted in clinical practice (eleuterococcus, ginseng family [Araliaceae], "gold root," etc.), administration of which for "pharmacohygienic" purposes [18], i.e., to maintain stable physical and mental efficiency for a long time in a healthy and active individual, elicits some effect. New products were also developed (phenatine, sydnocarb, sydnophen, piridrol, meridil, etc.) that could be considered as fast-acting stimulants [3-8, 40, 41, 43, 55, and others]. The products were submitted to comprehensive investigation as to their clinical applications, and several works have demonstrated their superiority to phenamine. At the present time, there are publications reporting the beneficial effects of PPA with simulant action and general tonics in the presence of fatigue as related to some types of activities [8. 13, 15, 20-22, 37, 65, 89, 103, 104, and others]. In the foreign literature, attention is concentrated primarily on various derivatives of amphetamines.

The pharmacodynamic properties of phenamine and its numerous analogues and derivatives are considered quite important from the standpoint of pathogenesis of disorders and probable functional disturbances associated with fatigue. The products stimulate such human qualities as optimism and self-confidence [100]; they increase efficiency in the case of sleep deprivation [89, 104] or markedly lowered motivation [65, 74, 80, 101]; they increase tolerance of conflict situations [85]; they improve significantly the quality of performance of tests that require stable motor coordination [72], etc. However, the unanimous opinion of specialists is that PPA of the phenamine type can be considered solely as emergency aids under particularly

difficult working conditions [22, 48, 58, 78, and others]. Regular intake of products in this group is absolutely inadmissible, since it depletes catecholamines in tissular reservoirs, with decrease in adaptive capabilities of the organism under sharply changing environmental conditions [9, 30, 62, 77, 87, and others].

Thus, data have now been accumulated, on the basis of which it is possible to make a primary selection of PPA with psychostimulant action to be followed by comprehensive experimental research on suitability thereof for aerospace medical practice.

Questions of optimizing the conditions under which man works and to maintain a high level of efficiency by means of regulating emotions with anxiolytic PPA were raised very recently in view of the discovery of this group of agents. The data published in recent years [2, 16, 22, 25, 31, 36, 39, 49, 75, 92, 97, and others) are indicative of the need for a very careful study of agents in this group from the standpoint of interests of aerospace medicine. Data are cited in the literature on the capacity of anxiolytics not only to alleviate subjective and autonomic components of emotional stress during intensive activity, but to retain efficiency to a significant extent.

Ruegg et al. [97], who tested the effect of elenium on fitness [efficiency] of candidates for pilots in the Swiss army, established that this product has an adverse effect on fitness only when taken in large doses (0.04 g). In doses of 0.01-0.02 g, elenium did not alter the capacity for concentration, complex psychomotor acts and other parameters.

The research of Patejdl et al. [91] revealed that meprobamate had a beneficial effect on shooting performance. O. S. Lobastov et al. [39] recommends elenium for riflemen that have a predisposition for nervous breakdowns. N. S. Kuz'mich et al. [36] obtained good results in their tests of trioxazine in paratroopers making jumps from low altitudes. V. P. Berezhnoy [16] reports that trioxazine is effective in lowering emotional tension of young soldiers during firing of guns. It was established that this agent attenuates autonomic reactions and improves the technical results of shooting.

Holliday [79], Davies [69] and others have reported the beneficial effect of anxiolytics on physiological reactions and efficiency in stress situations.

Apparently, the beneficial effects of these agents on efficiency are related primarily to their capacity to preserve purposeful tension at an optimum level, exceeding which results in disorganization of performance of the operator [42, 57, 76, 84, and others].

Analysis of the literature describing the pharmacological properties of the most popular representatives of anxiolytics reveals that not all of them are of equal interest to experimental investigation related to objectives of aerospace medicine. All of the products in this group (with the exception of trioxazine) are characterized in the literature as not being safe for individuals whose occupation requires rapid mental and motor reactions [1, 2, 40, 54, and others]. For example, according to the data of L. Kosha [34],

the advantage of trioxazine over other anxiolytics is that while it does lower overexcitability, inhibit impulsive emotional reactivity, eliminate fear and depression, its toxicity is very low and, in therapeutic doses, it does not induce drowsiness, listlessness, depression of intellectual activity and it does not have a myorelaxant effect or other undesirable effects. The myorelaxant action that is inherent in most anxiolytics, which induce either drowsiness (elenium, seduxen, meprobramate) or impairment of vision (amizil) is unquestionably one of their undesirable side-effects. In this regard, the warnings of many authors [56, 68, 82, 102, and others] about the danger of having flight personnel take various pharmacological agents with marked side-effects must be considered completely justified.

However, it should be borne in mind that this group of agents was investigated primarily in the aspect of clinical medicine. The described undesirable side-effects are usually demonstrable in the spectrum of pharmacological activity when large doses are prescribed or when they are taken regularly for a long period of time. There has not been sufficient investigation of the effects of single preventive intake of anxiolytics by healthy individuals. There is virtually no information in the literature about studies dealing with enhancement of beneficial aspects and attenuation of undesirable ones in the spectrum of pharmacological activity of anxiolytics. The question of choice of agent to curb the negative effects due to emotional tension of diverse genesis has not yet been definitively answered. In the opinion of A. V. Val'dman [19], Dews [71] and others, pharmacological regulation should be implemented with agents varying in type of action, depending on the nature of the provocative factor and neurophysiological mechanisms that are functional at a given stage of development of the stress reaction.

The solution to these and a number of other pressing problems of psychopharmacology will aid in successful implementation of clinical use of PPA with anxiolytic action.

The answer to the question of choice of PPA that would be suitable for their purpose implies the purposeful synthesis of new substances with predetermined spectrum of pharmacological activity, on the basis of medicotechnical specifications that are being worked out and choice of agents among those that have been well-studied and submitted to extensive clinical trial.

According to the data of Berde [61], it takes 7-11 years to develop a new drug, which requires considerable expense and labor. According to this author, just to advance this process to the stage of clinical investigation requires a mean of 150 man-years in labor units. The second direction also cannot be limited to simple choice of agents on the basis of data in the literature, and it will require special experimental research with due consideration of the specific conditions under which the products plan to be used. In our opinion, PPA intended to correct an altered functional state in pilots and astronauts during flights should, first of all, be

free of any deleterious effects on professional efficiency and endurance of typical stressors of aerospace flights; they should be in suitable form and easily administered; their toxicity must be low and they must have a wide therapeutic range of action; they should provide for rapid onset and long enough duration of expected therapeutic effect; there should be no deleterious reactions in the residual effects, etc.

It is quite probable that there will be some difficulties in choosing PPA that would meet all of the above requirements. They can be overcome by pinpointing exact dosage and time of administration, developing formulas consisting of products with different pharmacodynamics, etc.

The material published in recent years indicates that some advances have already been made in this direction. It has been demonstrated in experiments on animals that PPA may have effects in different directions on resistance of the organism to specific flight stressors [11, 12, 17, 22, 38, 44, 72, 90, and others]. The direction and intensity of the effect are determined by the spectrum of pharmacological activity of the product, its dosage, time and route of administration, characteristics of active factor, initial functional state of the organism and a number of other conditions. What is of basic importance is that one can increase resistance of the organism to various stressors by selecting the proper agent and dosage. The above effect was demonstrated when both stimulant and anxiolytic PPA were studied. A number of studies conducted on man [14, 20-22, 97 and others] demonstrated that it is possible to control the body's reactions to flight stressors: accelerations, altered gas environment, emotional stress, and fatigue against the background of prolonged monotonous activity. A remarkable finding made in the course of the studies is that the same positive results can be obtained by addressing oneself to different elements of physiological regulation using agents with different directions of pharmacodynamics. These data served as the basis for simultaneous, combined use of various analeptics and psychostimulants.

In the opinion of some authors [35, 70, and others], development of combined products that act simultaneously on various regulator and executor elements of the organism is a rather promising direction.

A number of authors have tried to combine agents with different pharmacodynamics in order to enhance their activity. For example, in France a new psychostimulant, debrumil is being advertised [64, 86]; it contains pyrrolizonecarboyxylic acid, demanol (alleviates synaptic transmission of excitation) and heptaminol (cardiovascular analeptic). Robelet and Lemoine [96] have also proposed a complex psychostimulant; V. S. Shashkov and N. V. Gordeycheva [582 propose a combination of ephedrine and strychnine; I. Iordanov [33] reports on the great efficacy of chinoxon, a Bulgarian combined product, which contains echinopsine base, vitamins B_1 and C, and phytin.

Our studies [22] demonstrated the advantage of a combination of caffeine, phenamine and strychnine (or securinine) over phenamine alone in the same dosage as in the formula. The compound stimulant has a stronger effect on

on central nervous system functions according to such criteria as antinarcotic effect, stimulation of motor activity, increased resistance to extreme physical loads, etc. In recents years, efforts are also being made to combine PPA with stimulant and anxiolytic action in order to normalize functions of the organs. This research was based on observations indicative of the possibility of obtaining the same positive results with products in these two groups [28, 88, 97, and others]. Furthermore, in his survey Evans [73] even voices the idea of relativity of making a distinction between psychostimulant and psychodepressant PPA. Some experimental data can serve as confirmation of this view. Thus, the studies of Bainbridge [60] showed that small doses of phenamine have a distinct sedative effect.

Hurst et al. [81] showed that amphetamine has a more potent "antipanic" effect than an effect of lowering the feeling of tiredness in fatigue. On the other hand, Yu. I. Vikhlyayev and T. A. Klygul' [24], V. V. Zakusov [29-32] and other authors demonstrated an activating component in anxiolytics of the benzdiazepine class and their ability to potentiate the stimulating effects of phenamine.

The combination of psychostimulant and anxiolytic PPA was used in experiments on animals and studies on man by G. D. Glod et al. [28], B. P. Shestkov [592, Cuthbertson and Knox [67], Quarton and Talland [94], Rushton and Steinberg [98], Hurst et al. [91], Cooper et al. [67], Quenzer et al. [95] and others. Simeon et al. [99] and other authors have reported on the use of such combinations in medical practice. The results of these studies have demonstrated the desirability and potential of this combined approach to problems of specific regulation of functional state of the organism.

The desirability of combined use of a psychostimulant and anxiolytic can be illustrated by the results of our research on the antihypoxic activity of separate and combined use of centedrine and trioxazine, according to which the antihypoxic activity of the combination is superior to that of separate use of the ingredients.

Even this brief analysis of the data in the literature illustrates the implications of a search for the ways and means of controlled regulation of function of the main physiological systems of the organism in the area of psychopharmacological agents. At this time, apparently only the serious prerequisites have been formulated for practical implementation of the problems discussed. Implementation of applied directions of psychopharmacology in aerospace medicine requires a systems approach, which combines the distinctive features of physiological, experimental psychological, ergonomic and other investigative methods in the laboratory and under actual conditions of man's performance. Adoption in practice of scientifically substantiated methods of psychopharmacological correction of functional state of crew members, when altered under the influence of separate or combined effects of space factors and working conditions, will be an important supplement to the existing measures referable to medical back-up of aviation and space flights.

The intensive development of modern psychopharmacology makes it imperative to pursue continuous and systematic studies both to assess the applicability

of new PPA to aerospace medicine and development of special products with preset properties.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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CONDITION OF MICROSCOPIC AND CRYSTALLINE STRUCTURES, MICROCONSISTENCY AND MINERALIZATION OF HUMAN BONE TISSUE FOLLOWING A LONG SPACE FLIGHT

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[Text] One of the rather pressing and important problems of space biology and medicine is the state of calcium metabolism in the organism under the influence of space flight factors. In spite of the advances of modern space biology and medicine, the problem of calcium metabolism during prolonged space flights is still relatively poorly developed, but it is quite important from the practical point of view, particularly in connection with prolonged manned flights on orbital stations.

Elevation of blood calcium content and increased excretion thereof in urine and feces, decreased mineralization of some skeletal bones (for example, the calcaneus) have been observed in astronauts who have participated in long orbital space flights [1-4].

There are a number of unanswered questions in this problem, that are related, to some extent, to the limited possibility of evaluating mineralization of bone tissue according to results of roentgenophotometric and ultrasonic studies, including their crystalline cancellus, protein matrices, proportion of organic and inorganic fractions and other properties that determine dynamic stability of bone tissue, the mechanism of effects of various space flight factors, as well as determination of compensatory capabilities of bone tissue under such conditions.

Methods

Our objective included comprehensive investigation of tissue of different skeletal bones: calcaneus, femoral epiphysis and diaphysis, body of the vertebra, rib and sternum (autopsy material from the crew of Salyut-1 station). We used a set of various techniques for more comprehensive and in-depth examination of this material: pathohistological, crystallographic, biophysical and biochemical.

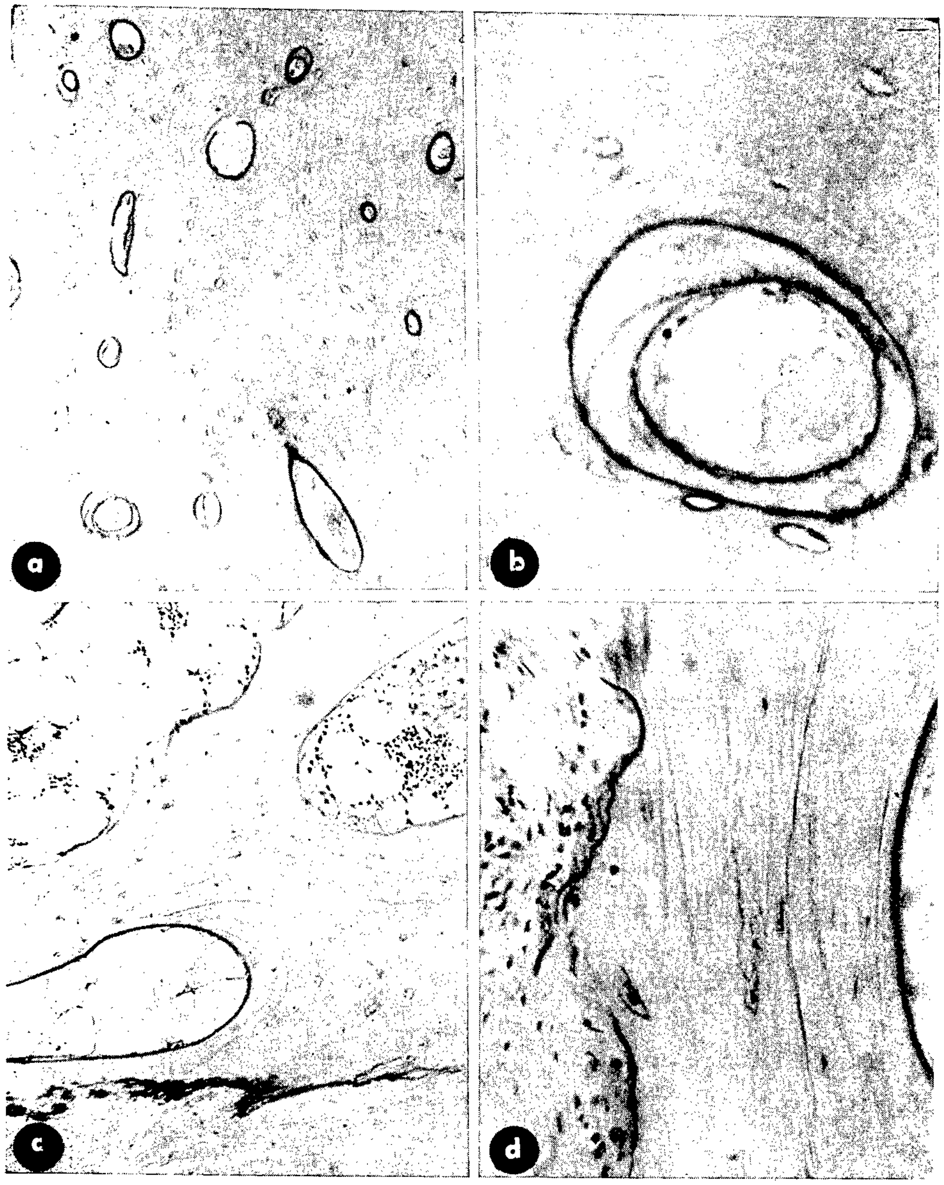

Figure 1. Compact and spongy bone tissue.
Bone substance of femoral diaphysis has a compact structure (a), well-developed osteonic structures (b). In the calcaneus there is a predominantly spongy type of structure; the compact lamella is very poorly developed; the medullary spaces contain yellow marrow (c); resorption niches and erosions are demonstrable in the compact lamella without signs of cellular osteoclastic reaction (d). Hematoxylin-eosin stain; magnification: 40× (a), 125× (b), 55× (c) and 100× (d).

A histopathological study was made of unadulterated [polished] sections, decalcified and hematoxylin-eosin stained sections of bone tissue. The crystallographic studies were made by means of x-ray analysis on an URS-50IM

roentgenodiffractometer [5]. Microhardness [microconsistency] of bone tissue samples was determined with a PMT-3 instrument using previously described techniques [6].

Soft tissues (cartilage, periosteum, marrow) were completely removed from bone tissue samples, formalin was removed, then lipids and carbohydrates in order to assay calcium and phosphorus content; we estimated the proportion (percentage) of protein and mineral fractions. Calcium content was assayed using a flame spectrophotometer and phosphorus with an SF-16 spectrophotometer.

Bone tissue of autopsy material taken from three men who had died of acute trauma at 20-40 years of age (without pathoanatomically demonstrable signs of pathology of internal organs and systems) served as the control for comparative analysis.

In order to obtain data with preset (at least 95%) degree of probability, the studies were programmed, using mathematical methods [7, 8], with determination of number of parallel tests and analyses, and other conditions. All of the obtained digital data were submitted to statistical processing by the method of Student to determine the degree of reliability.

Results and Discussion

Pathohistological examination revealed structures corresponding to the type of bone examined in preparations of bone tissue. There were elements of compact and spongy bone. Well-developed compact bone structures are demonstrable in the femoral diaphysis. In the other bone fragments the compact substance forms a thin external compact lamella that changes into spongy bone matter toward the middle. In all preparations, bone is represented by well-developed osteon structures formed by bone plates concentrically arranged around blood vessels. Three layers of compact substance are distinct in the femoral diaphysis: external and internal layers of basic ["general"] lamellae and a middle osteonic layer. Here and there in the external layer Volkmann's canals are visible. Mildly basophilic lines are demonstrable between layers and different osteon systems of the middle layer. The lines of adhesion in the external layer are parallel to the bone surface and more intensively stained. The spongy substance of bone also presents osteonic structure. The Haversian systems of compact and spongy bone contain dilated plethoric vessels. In some areas over the surface of compact lamellae, shallow erosions and niches can be seen in the margin of bone trabeculae, without signs of a cellular osteoclastic reaction (Figure 1).

The medullary lacunae in the spongy substance of the epiphysis and calcaneus are filled with yellow marrow represented by extremely friable honeycomb-like substance formed by fat cells, between the well-developed, thick trabeculae. In the medullary lacunae of the spongy substance of the body of the vertebra, there are elements of red marrow represented by cells of the myeloid class, reticular cells, as well as giant cells, i.e., megakaryocytes. Here and there inclusions of fat cells are seen. The vessels of the yellow and red

marrow are dilated and injected with blood. In some preparations there is significant plethora (Figure 2, a and b).

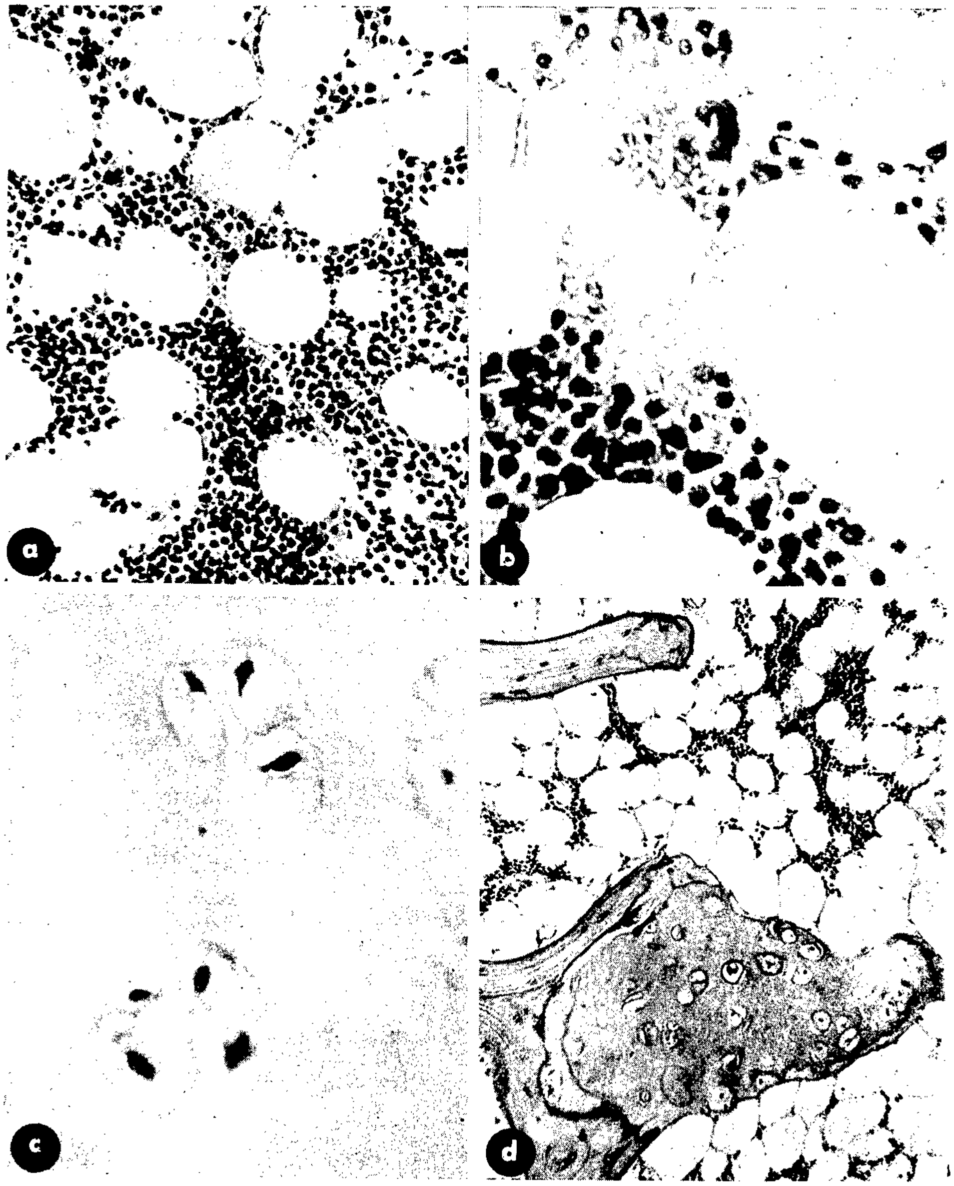

Figure 2. Bone marrow and cartilaginous tissue
Medullary lacunae of rib filled with red marrow (a). Red marrow cells of body of vertebra represented by elements of the myeloid class; isolated megakaryocytes are encountered (b). The cartilage of the articular surface of the femoral epiphysis has a structure of the hyalin type (c). There is a mature cartilage island in the spongy substance of sternal bone tissue (d). Hematoxylin stain; magnification: 40× (a, d) and 125× (b, c).

Table 1. Microhardness of bone tissue (kg/cm^2)

Skeletal bone	Index	Type of bone tissue: compact	spongy
Calcaneus	SF [space flight]	46,9±0,7	44,2±0,7
	Normal	46,3±0,6	46,5±0,5
	Difference [diff.]		
	kg/cm^2	+0,6	−2,3
	% of normal	+1,3	−4,9
	Reliability of diff:		
	t	0,7	2,6
	P	>0,05	<0,02
Epiphysis of femur	SF	44,9±0,5	50,7±0,5
	Normal	44,1±0,5	46,0±0,7
	Diff.:		
	kg/cm^2	+0,8	+4,7
	% of normal	+1,8	+10,2
	Reliability of diff.		
	t	1,0	5,3
	P	>0,06	<0,01
Diaphysis of femur	SF	53,8±0,7	53,9±0,7
	Normal	51,0±0,8	56,2±0,7
	Diff.:		
	kg/cm^2	+2,8	−2,3
	% of normal	+5.5	−4.1
	Reliabil.of diff.:		
	t	2,5	2,2
	P	<0,05	0,05
Vertebral body	SF	43,6±0,7	44,4±0,4
	Normal	40,1±0,6	42,4±0,6
	Diff.:		
	kg/cm^2	+2,5	+2,0
	% of normal	+8,7	+4,7
	Reliabil.of diff.:		
	t	3,7	2,9
	P	<0,01	<0,02
Sternum	SF	41,7±0,5	39,8±0,6
	Normal	43,0±0,5	42,5±0,5
	Diff.:		
	kg/cm^2	−1,3	−2,7
	% of normal	−3,0	6,4
	Reliabil.of diff.:		
	t	1,8	3,4
	P	0,05	<0,01
Rib	SF	43,6±0,6	45,6±0,5
	Normal	39,2±0,5	40,6±0,5
	Diff.:		
	kg/cm^2	+4,4	+5,0
	% of normal	+11,2	+12,3
	Reliabil.of diff.:		
	t	7,2	6,7
	P	0,001	0,001

Note: Here and in Tables 2-4, SF--space flight.

Table 2. Mineral fraction (ash) of bone tissue (% dry weight)

Skeletal bone	Index	Bone tissue: overall	compact	spongy
Calcaneus	SF	64,4±0,7	65,0±1,1	63,7±0,7
	Normal	65,5±0,6	65,3±0,8	65,7±1,0
	Difference	—1,1	—0,3	—2,0
	Reliab.of diff.:			
	t	1,2	0,2	1,7
	P	>0,05	>0,05	>0,05
Epiphysis of femur	SF	67,8±0,7	68,2±0,9	67,5±1,2
	Normal	68,1±0,8	69,7±0,2	66,5±1,5
	Diff.	—0,3	—1,5	+1,0
	Reliab.of diff.:			
	t	0,3	1,7	0,5
	P	>0,05	>0,05	>0,05
Diaphysis of femur	SF	68,6±1,5	71,5±0,4	63,3±2,7
	Normal	71,4±0,1		
	Diff.	—2,8		
	Reliab.of diff.:			
	t	1,9		
	P	>0,05		
Vertebral body	SF	55,9±3,6	66,1±0,1	57,1±1,2
	Normal	52,8±1,1	56,1±1,5	51,2±0,7
	Diff.	+3,1	+10,0	+5,9
	Reliab.of diff.:			
	t	1,0	6,7	4,2
	P	>0,05	<0,001	<0,001
Sternum	SF	58,6±1,8	64,3±1,5	53,4±0,7
	Normal	56,8±2,5	62,2±0,9	51,4±1,5
	Diff.	+1,8	+2,1	+2,0
	Reliab.of diff.:			
	t	0,6	1,2	1,2
	P	>0,05	>0,05	>0,05
Rib	SF	63,7±2,5	68,0±0,8	53,6±4,3
	Normal	64,4±2,1	67,6±0,5	55,0±1,6
	Diff.	—0,7	+0,4	—1,4
	Reliab.of diff.:			
	t	0,2	0,4	0,3
	P	>0,05	>0,05	>0.05

Cartilaginous tissue is demonstrable in preparations of femoral epiphysis. The localization of the cartilage corresponds to the articular surface of the bone. Structurally, the cartilage is of the hialine type. The cartilaginous cells are diverse in shape, mainly oval, and elongated only near the cartilage surface. The intercellular substance is amorphous and markedly basophilic (Figure 2c).

In one of the histological preparations of sternal tissue, islands of mature cartilage varying in size are demonstrable in the spongy substance of the manubrium, which is often intimately related to the substance of the osseous trabeculae. At the same time, some parts of this cartilage

present dystrophic changes and it is invaded by capillary type blood vessels; the impression is gained that there is enchondral replacement of cartilage with osseous structures (Figure 2d).

Table 3. Calcium content of bone tissue (% of ash)

Skeletal bone	Index	Bone tissue		
		overall	compact	spongy
Calcaneus	SF	36,1±0,1	35,5±0,1	35,5±0,1
	Normal	36,1±0,1	36,0±0,2	36,2±0,2
	Difference	0	—0,5	+0,3
	Reliab.of diff.:			
	t	0	2,6	1,4
	P	>0,9	<0,02	>0,1
Epiphysis of femur	SF	37,1±0,1	37,2±0,2	37,0±0,2
	Normal	36,7±0,1	36,5±0,1	36,9±0,1
	Diff.	+0,4	+0,7	+0,1
	Reliab.of diff.:			
	t	0,2	1,3	0,1
	P	>0,8	>0,1	>0,9
Diaphysis of femur	SF	36,7±0,3	37,3±0,6	
	Normal	35,4±0,2	34,6±0,1	
	Diff.	+1,3	+2,7	
	Reliab.of diff.:			
	t	0,8	4,7	
	P	>0,4	<0,001	
Vertebral body	SF	36,6±0,2	35,8±0,1	
	Normal	35,4±0,1	36,4±0,4	
	Diff.	+1,2	—0,6	
	Reliab.of diff.:			
	t	6,0	1,2	
	P	<0,001	>0,1	
Sternum	SF	35,8±0,3	36,3±0,3	35,5±0,5
	Normal	36,1±0,1	36,2±0,1	36,1±0,3
	Diff.	—0,3	+0,1	—0,6
	Reliab.of diff.:			
	t	1,0	0,5	1,0
	P	>0,3	>0,6	>0,3
Rib	SF	36,0±0,2	35,8±0,3	36,6±0,4
	Normal	35,2±0,2	35,6±0,2	34,2±0,5
	Diff.	+0,8	+0,2	+2,4
	Reliab.of diff.:			
	t	2,9	0,6	1,2
	P	<0,01	>0,5	>0,2

The external layer of bone fragments is covered with periosteum, which consists of two layers: fibrous and adventitial. There are blood vessels and osteoblasts in the internal layer. The external layer of periosteum consists of compact connective tissue containing coarse bundles of collagen fibers. Blood vessels traverse this layer also. Thus, the described histological findings correspond to variants of microscopic structure of normal human skeletal bones.

Table 4. Phosphorus content of bone tissue (% of ash)

Skeletal bone	Index	Bone tissue		
		overall	compact	spongy
Calcaneus	SF	16,4±0,1	16,0±0,1	16,4±0,1
	Normal	15,6±0,1	16,1±0,2	15,0±0,1
	Difference	+0,8	−0,1	+1,4
	Reliab.of diff.:			
	t	7,9	0,5	10,0
	P	<0,001	>0,6	<0,001
Epiphysis of femur	SF	16,4±0,1	16,4±0,1	16,5±0,1
	Normal	15,9±0,2	16,1±0,2	15,7±0,3
	Diff.	+0,5	+0,3	+0,8
	Reliab.of diff.:			
	t	2,5	0,1	3,1
	P	<0,02	>0,9	<0,01
Diaphysis of femur	SF	16,5±0,1	16,6±0,1	
	Normal	15,0±0,1	15,4±0,1	
	Diff.	+1,5	+1,2	
	Reliab.of diff.:			
	t	12,0	8,5	
	P	<0,001	<0,001	
Vertebral body	SF	16,6±0,1	16,5±0,1	
	Normal	14,6±0,1	14,5±0,2	
	Diff.	+2,0	+2,0	
	Reliab.of diff.:			
	t	14,2	9,5	
	P	0,001	0,001	
Sternum	SF	16,1±0,1	16,0±0,1	16,1±0,1
	Normal	15,1±0,4	15,8±0,5	14,1±0,2
	Diff.	+1,0	+0,2	+2,0
	Reliab.of diff.:			
	t	2,4	0,4	10,0
	P	<0,02	>0,6	<0,001
Rib	SF	16,8±0,2	16,6±0,1	16,6±0,1
	Normal	14,9±0,1	14,9±0,1	14,9±0,1
	Diff.	+1,9	+1,7	+1,7
	Reliab.of diff.:			
	t	8,2	12,1	12,1
	P	<0,001	<0,001	<0,001

Crystallographic studies, based on interpretation of roentgenodiffractograms [9] revealed that the interplanar distances correspond to a mixture of hydroxylapatite, fluorapatite, tricalcium phosphate, etc., in the examined specimens of calcaneal bones following a space flight. Nevertheless, in these samples, there are more distinct (as compared to normal) lines that are typical for hydroxylapatite, carboyslapatite and tricalcium phosphate. This is indicative of more marked crystallization than in control samples.

The interplanar distances, as well as parameters of elementary cell of apatite crystals, are very similar in values. For this reason, the lines of interplanar distances are overlapped on the roentgenodiffractograms, so that we cannot clearly determine whether there is prevalence of any type of apatite.

Thus, the delineation of crystalline structures of bone tissue in the group under study is somewhat greater than in the control group. According to the studied parameters of the crystalline structure, it can be considered that there are more active processes of crystallization in bone tissue of the group in question than in the control group.

Analysis of microhardness of normal bone tissue (control group) revealed that the microhardness levels are the same for compact and spongy bones of all skeletal bones studied (with the exception of the femoral diaphysis), and there are no appreciably reliable differences. Microhardness of the diaphysis of the femur (both compact and spongy parts) is an average of 12.5% greater than in other skeletal bones. These data are consistent with the literature [10].

A comparison of microhardness of bone tissue in the studied and control groups failed to demonstrate substantial differences. The existing differences between microhardness indices of homologous bones in the studied and control groups fluctuate over a few percentage points, which could be attributed to individual variability and permissible range of error of the methods used (Table 1). The demonstrated statistically reliably and substantial differences, in the direction of increased microhardness of some bones, for example the femoral epiphysis, rib and others, can apparently be interpreted as some increase in strength of these bones, related for example to intensive physical training, accelerations, etc., which do not have an appreciable effect on their function.

The mineral fraction of bone tissue (both compact and spongy), as well as proportion thereof in relation to the protein fraction, did not differ appreciably from normal (control group) in all bones examined. In the test group, there was some elevation (by 5.9-10.0%) of mineral content in the vertebral body, as compared to normal (Table 2).

A study of calcium content failed to demonstrate differences from normal in any of the bones examined. There are statistically reliable deviations, in the range of 0.5-0.8-1.2-2.70, as compared to normal, which can be interpreted as individual fluctuations, as well as permissible error factor of the method (Table 3).

A study of phosphorus content of bone tissue revealed differences, in the direction of 0.5-2.0% increase, as compared to normal, and there was a rather high degree of reliability in a number of cases (99.99%; Table 4).

Comparative analysis of the results of these comprehensive studies of bone tissue of the human skeleton following a prolonged space flight, using various methods, demonstrated a clearcut correlation according to the indices studied. Pathohistological studies and x-ray analysis revealed that the microscopic and crystalline structures of bone tissue in all skeletal bones examined do not differ from normal (control group). There was also a distinct consistency between indices of microhardness and mineralization (ash, calcium and phosphorus) of skeletal bone tissue, which are within the normal range.

No appreciable deviations from normal that could have been interpreted as pathological were demonstrable according to all parameters studied. The changes in the direction of consolidation of the crystalline lattice of bone tissue, increased microhardness and mineralization can most likely be attributed to the effect of physical loads and training [conditioning]. On the basis of analysis of the literature and results of these studies it is difficult to derive a definite conclusion to explain the substance of the data obtained at this time. For this reason, we shall merely expound an assumption (as a working hypothesis) that the normal condition of bone tissue of the human skeleton following a prolonged space flight could be due to a high level of physical training and conditioning of astronauts and subsequent use of the set of equipment and conditioning measures onboard the Salyut-1 orbital station, that were directed toward precluding the undesirable effects of weightlessness and hypokinesia on the human body during orbital space flights.

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DISTINCTIVE FEATURES OF REGIONAL CIRCULATION AND VASOMOTOR REGULATION FOLLOWING A TWO-MONTH SPACE FLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 20-26

[Article by Kh. Kh. Yarullin and T. D. Vasil'yeva, submitted 26 Apr 76]

[Text] Redistribution of blood in the body is one of the main mechanisms of regulation of adequate blood supply to organs and tissues. In the presence of regional circulatory disorders, for example in the brain, there is also redistribution of blood in different vascular reservoirs, to compensate for the hemodynamic changes and to maintain homeostasis. It is particularly interesting to study vasomotor regulation and regional hemodynamics of astronauts during and after space flights in view of the significant redistribution of blood in the body under the influence of weightlessness. In this report, we submit the results of rheographic investigation of regional hemodynamics in the crew of Soyuz-18 and Salyut-4 before and after a 2-month orbital flight.

Method

During passive orthostatic and antiorthostatic tests we recorded synchronously rheoencephalograms (REG) in the frontomastoidal and bimastoidal leads, which reflects pulsed flow [filling], elasticity and tonus of vessels in the system of the internal carotid artery and vertebrobasilar system, as well as rheograms (RG) of the right lung and crus, photoplethysmogram (PPG) of the third finger and EKG in the second standard lead. Under basal metabolic conditions, we also tested RG of the liver, forearm, fingers and toes. Studies under basal metabolic conditions were pursued before the flight and on the 1st, 3d, 16th and 40th (59th) days after landing. The method used to analyze the RG was described previously [7]. The orthostatic test was performed with the table turned at an angle of +70° for 10 min, and the antiorthostatic one, at angles of -15° and 30° for 6 min. The orthostatic and antiorthostatic tests were performed once before the flight, on the 1st, 3d, 7th, 14th and 40th (56th) postflight days.

Results and Discussion

The rheographic studies under basal metabolic conditions revealed more or less marked changes in regional hemodynamics both after the 2-month and 1-month orbital flights. On the 1st postflight day, P. I. Klimuk presented distinctly lower tonus of arterioles and veins in the system of the internal carotid: as compared to preflight values, there was a 23.6-28% decline of dicrotic (DCI) and diastolic (DSI) indices of the REG. The diminished vascular tonus was associated with 20% decrease in pulsed filling of the left hemisphere. In the vertebrobasilar system arteriolar and venous tonus was increased to the normal level and there was some increase in pulsed filling. In V. I. Sevast'yanov, we observed diminished tonus of arterioles and veins in the right hemisphere (DCI of hemispheric REG dropped from 51.5 to 21.2%; DSI, from 54.6 to 17.5%) and vertebrobasilar system (DCI of occipitomastoidal REG dropped from 36.3 to 18.7%, and DSI, from 41.1 to 21.4%) with minor decrease in vascular tonus of the left hemisphere. Pulsed filling of cerebral vessels in all three reservoirs studied, as well as of the lung and finger, was significantly increased (by 60-100%, particularly in the left hemisphere). As we see, both cosmonauts presented distinctly asymmetrical pulsed filling and cerebrovascular hypotension. Yet, on the 1st day after a 1-month flight, A. A. Gubarev and G. M. Grechko presented increased tonus of cerebral arterioles and veins (DCI of REG rose to 91.5-100% and DSE, to 103.5-110%). The preflight DCI and DSI did not exceed 44.3 and 33.%, respectively, in the former cosmonaut and 77.5 and 87.6%, in the latter. In other words, both cosmonauts presented signs of cerebrovascular, particularly venous, i.e., postcapillary hypertension [1, 4, 15, 17]. There was also prevalence of signs of venous hypertension in the lungs and liver of G. M. Grechko, venous and arteriolar hypotension in the liver and crus of A. A. Gubarev.

In P. I. Klimuk and V. I. Sevast'yanov, the signs of vascular hypotension of the leg and toes, particularly venous, were much less marked, in spite of their 2-month flight, than in A. A. Gubarev and G. M. Grechko. Thereafter, the indices of tonus of precapillary and postcapillary vessels of the crus came close to preflight levels as early as the 17th day of the readaptation period in the crew of the second expedition, whereas in the crew of the first expedition these indices remained overtly low, even on the 30th day. At the same time signs of deposition of blood in the lungs and liver were more marked in P. I. Klimuk and V. I. Sevast'yanov.

Apparently the sharp increase in pulsed filling of the finger after the flight, against the background of significant increase in vascular tonus, in A. A. Gubarev and G. M. Grechko is due not only to redistribution of blood, but entrance of tissular fluid into the capillary stream. The relative prevalence of vasodilatation could have induced increase exit of fluid from capillaries [4, 17], which was observed in P. I. Klimuk and V. I. Sevast'yanov. The demonstrated difference in mechanisms of increasing blood supply to the finger is apparently due to successful adjustment of changes in fluid and sodium metabolism which occurred during the 2-month flight of P. I. Klimuk and V. I. Sevast'yanov and succeeded in effectively normalizing vascular tonus and capillary circulation, i.e, the microcirculatory system [2, 12, 17].

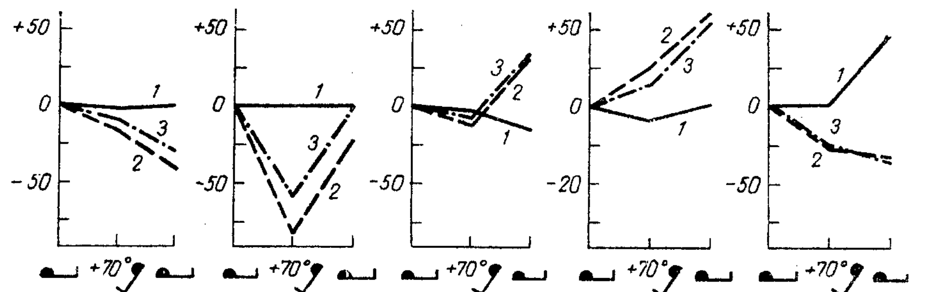

Figure 1. Dynamics of changes in maximum amplitude (1), dicrotic (2) and diastolic (3) indices of bimastoidal REG in P. I. Klimuk during orthostatic test before and after 2-month flight (%)

The prevalence of vasoconstrictive reactions in A. A. Gubarev and G. M. Grechko for the first 3 postflight days could be attributed, to some extent, to adaptive increase in tonus of peripheral vessels, which aided in maintaining adequate circulation in the presence of a decreased circulating blood volume [13]. The effective correction of changes in fluid and sodium metabolism of P. I. Klimuk and V. I. Sevast'yanov at the end of the flight was instrumental in some degree of restoration of circulating blood volume and, consequently, predominance of vasodilator reactions. Asymmetry of vascular tonus of the hemispheres in V. I. Sevast'yanov and P. I. Klimuk could have been due to either individual distinctions of vascular tonus and reactivity or development of vegetovascular dysfunction, i.e., more or less marked change in function of vasomotor centers. The changes in vascular reactivity and tonus could have been induced, particularly during the antiorthostatic test, by the direct effect of fluctuations of intracranial pressure on hypothalamic and stem vegetative elements that regulate vascular tonus.

The most marked changes in cerebrovascular reaction to postural factors were demonstrable in P. I. Klimuk on the 1st postflight data. As can be seen in Figure 1, the orthostatic test was associated with a drop of DCI (by 81%) and DSI (by 60%) on the bimastoidal REG. Signs of arteriolar and venous hypotension in the vertebrobasilar system were associated with weakness, vertigo, as well as nausea, particularly when turning and bending the head. Signs of difficult efflux and venous stasis were demonstrated on the RG of the lower leg. In spite of this, the entire test was performed. Evidently, concurrent compensatory increase in pulsed filling of the internal carotid (by 36.8%) aided in maintaining the critical level of blood supply to the brain, for which reason there was satisfactory endurance of the test.

At the same time, in cosmonaut A. A. Gubarev, a similar decrease in vascular tonus, particularly arteriolar, in the vertebrobasilar system was associated with appreciable decrease in pulsed delivery of blood to the brain (Figure 2).

Already in the 1st min of being in vertical position, there was a decrease in arteriolar tonus, both in the hemispheres and vertebrobasilar system (DCI dropped from 85.2 to 10-11.5% and DSI, from 83.3 to 47.5-27.4%), and this was associated with 32.5% decrease in pulsed delivery of blood. Hypotension of cerebral vessels and arterioloparesis were associated, from the 4th min on, with very rapid elevation and sharp decline of REG wave, with increase in its amplitude. Evidently, the cerebral vessels, having lost their elasticity and capacity to contract, reacted passively to the fluctuations of systemic arterial pressure. All this was associated with weakness, mild nausea and profuse cold perspiration, i.e., development of a precollaptoid state. For this reason, the table was moved to horizontal position after 4 min and 15 s.

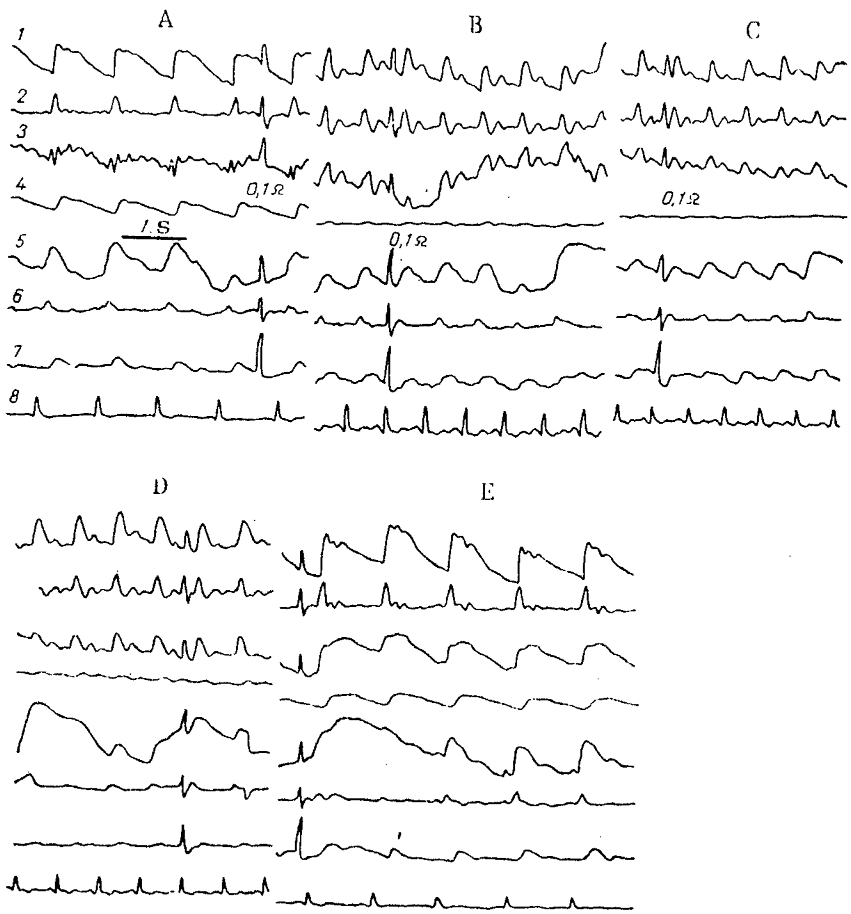

Figure 2. Dynamics of frontomastoidal (1) and bimastoidal (3) REG, derivatives of hemispheric REG on the right (2) and RG of the lung (6); photoplethysmogram of the finger (4), RG of right lung (5) and lower leg (7), and EKG (8) of A. A. Gubarev before and during orthostatic test on 1st postflight day.

A) background tracing in horizontal position
B) 1st min of vertical position
C) 3d min
D) 5th min of vertical position
E) recovery period in horizontal position

In P. I. Klimuk, the vertebrobasilar system was found to be less resistant to antiorthostasis as well on the 1st postflight day (Figure 3). Compensatory increase in arterioral tonus of this system was less marked than before the flight, while venous tonus even diminished, and this was associated with passive increase in pulsed delivery of blood (by 172% at -15° angle and 260% at -30°; 73.2 and 100%, respectively, before the flight), i.e., development of subcompensated venous stasis. More marked passive cerebral hyperemia during antiorthostasis on the 1st postflight day is indicative of local impairment of autoregulation of hemodynamics in the vertebrobasilar system.

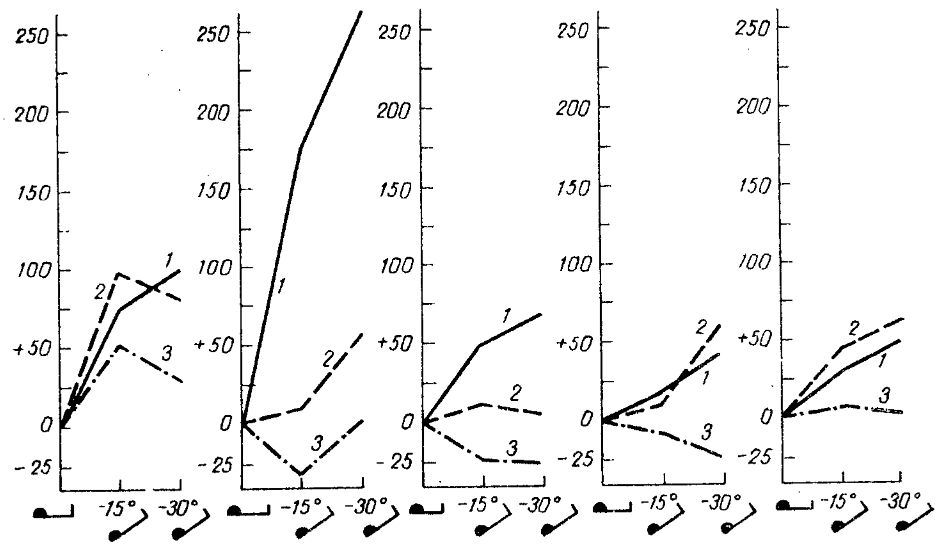

Figure 3. Dynamics of changes in maximum amplitude (1), dicrotic (2) and diastolic (3) indices of bimastoidal REG of P. I. Klimuk during antiorthostatic load before and after 2-month flight (%)

Since worsening of well-being of P. I. Klimuk and A. A. Gubarev during the orthostatic test was preceded by a decrease in tonus of arterioles and veins in the vertebrobasilar system, there is reason to believe that impairment of autoregulation of hemodynamics in this reservoir is one of the triggering mechanisms of decreased orthostatic stability. The possibility cannot be ruled out that the vestibular disorders observed in P. I. Klimuk during and after the flight are related to the above-described hemodynamic disturbances in the vertebrobasilar system. It is known that even minor changes in blood pressure or decreased flow of blood in the internal auditory arteries, which are branches of the basilar artery, can induce vestibular disorders [16]. Furthermore, P. I. Klimuk presented signs of arteriolar and venous hypotension in the vertebrobasilar system following an 8-day flight as well.

In V. I. Sevast'yanov, orthostasis on the 1st postflight day was associated with decrease in pulsed delivery of blood (by 48.5%) and in tonus of cerebral

arterioles and veins, which was more marked in the reservoir of the internal carotid (DCI and DSI of hemisphere REG diminished by 32%). The 433% elevation of diastolic index of the RG of the lower leg during the orthostatic test on the 1st postflight day was indicative of plethora of the veins, apparently due to diminished elasticity and tonus of deep veins of the crus [9, 11]. This elicited a sharp compensatory increase of arteriolar tonus and restricted arterial influx to a greater extent than before the flight. Consequently, orthostatic endurance was also diminished in V. I. Sevast'yanov, but to a lesser extent than in P. I. Klimuk. In both cosmonauts, signs of plethora of the brain during the antiorthostatic test were appreciably more marked than before the flight. In the crew of Soyuz-17 and Salyut-4, on the 1st postflight day considerably less increase in cerebral filling was noted in antiorthostasis than before the flight, whereas in the vertebrobasilar system there were fewer or no changes against the background of distinctly increased arteriolar and venous tonus. These residual compensatory reactions of cerebral hemodynamics gradually disappeared by the 7th postflight day in A. A. Gubarev and G. I. Grechko. With repetition of antiorthostatic tests, there was improved tolerance of the tests by P. I. Klimuk and V. I. Sevast'yanov. This was manifested by a lesser increment of pulsed delivery of blood, against the background of marked compensatory increase in tonus of cerebral vessels, which limited passive cerebral hyperemia in antiorthostatic position. The manifestations of adaptation of cerebral vessels toward the 2d month of weightlessness were the most marked on the 16th postflight day and leveled off by the 40th day. Endurance of orthostatic position gradually improved in both cosmonauts and was close to the preflight level on the 16th day of the readaptation period.

There was less change in α/T (%) (tonus index, mainly of large and medium caliber vessels) under the influence of postural factors, as well as at rest, than in DCI and DSI; not infrequently it presented minimal changes. It rose reliably only with a sharp decrease of tonus of cerebral arterioles and veins during antiorthostasis. Apparently this increase in tonus of arteries of large caliber was compensatory and directed toward providing hemodynamic homeostasis in the presence of significant decrease in arteriolar and venous tonus.

On the 30th postflight day, DCI and DSI remained low on the RG of the leg and PPG of the finger of A. A. Gubarev and G. M. Grechko. Since the DCI reflected the state of precapillary fine vessels and DSI, that of postcapillary ones [1, 3, 5, 6, 8, 10, 14, 17] the above signs of arterial and venous hypotension were indicative of microcirculatory changes, particularly in regions with less capacity for self-regulation.

At the same time, the results of rheographic studies of regional hemodynamics during postural tests demonstrated weakening of mechanisms of self-regulation of cerebral circulation for the first 3 days after returning to earth. This was manifested by diminished orthostatic stability and even development of collapse in A. A. Gubarev at the very start of the orthostatic test, as a result of diminished tonus of cerebral vessels, particularly arterioles, and signs of vasoparesis, mainly in the vertebrobasilar system which was also

less stable before the flight. As a result, arterial ischemia of the brain was complicated by circulatory venous ischemia and led to decompensation of self-regulation of cerebral blood flow and of the cardiovascular system as a whole. Since a decline of DCI on the PPG of the finger, from 86% to 0, against the background of minor decline of DSI (from 86 to 62%), preceded development of the presyncopic state, it can be assumed, with a high degree of probability, that the significant decrease in tonus and contractility of fine precapillary vessels, i.e., arterioles and precapillaries, is one of the mechanisms of development of orthostatic hypotension, since the tonus of fine postcapillary vessels remained rather high.

The prolonged persistence of sequelae of adaptation of cerebral vessels to stress factors related to weightlessness is indicative of the fact that a new stable state of cerebral hemodynamic homeostasis was obtained by the end of the 2-month flight.

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STUDIES OF CIRCULATION DURING LBNP TEST ABOARD SALYUT-4 ORBITAL STATION

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[Article by V. A. Degtyarev, V. G. Doroshev, T. V. Batenchuk-Tusko, Z. A. Kirillova, N. A. Lapshina, S. I. Ponamarev and V. N. Ragozin, submitted 21 Sep 76]

[Text] The functional test using lower body negative pressure (LBNP) is used constantly in the system of medical monitoring of astronauts [1, 2]. Studies conducted during preflight preparations [3, 4] and in weightlessness [5] confirmed that this test is informative in determining orthostatic endurance of the crews. However, there are still some problems to be solved: mangitude of decompression used, frequency of tests, distinctions of circulatory reactions to LBNP in weightlessnes, criteria of endurance thereof, etc.

The functional test with LBNP was conducted on the Salyut-4 orbital station in order to evaluate and predict orthostatic endurance of cosmonauts.

Methods

LBNP tests were conducted three times in the preflight period: 94, 67 and 8 days before the flight.

During the flight on Salyut-4 orbital research station, P. I. Klimuk performed the test 9 times (on the 14th, 18th, 22d, 28th, 31st, 37th, 44th, 53d and 60th days) and V. I. Sevast'yanov, 10 times (19th, 14th, 22d, 27th, 31st, 37th, 43d, 53d, 60th and 61st days).

A comprehensive study of circulation with LBNP was conducted five times on each cosmonaut. After landing, the test was made in 6 h (0 day), 4th and 6th days. LBNP was created by immersing the subject in a Chibis pressure suit. For the first 2 min of the test, pressure was lowered by 25 mm Hg, in relation to ambient level, and by 35 mm Hg in the next 3 min. Before, during the test and during the recovery period, we recorded the tachyoscillogram (TO) and distal perimetric oscillogram (DPO) of the brachial artery, kinetocardiogram (KKG) in the region of the apex beat and

sphygmogram of the femoral artery (SPG). We measured the rate of cardiac contractions, arterial pressure, velocity of pulse wave (PWV) in the aorta, phases of cardiac cycle in the left ventricle. We calculated stroke and minute blood volumes, specific actual and standard [proper] peripheral resistance of vessels.

The inflight data were compared to all preflight test results, but the graphs included results of a test made 8 days before the flight, since it was conducted in the same climate zone and under the same conditions as the postflight studies.

Results and Discussion

The cosmonauts had no complaints during LBNP; their heart rate increased by 30-36%, minute volume decreased by 20-37% and stroke volume by 33-45%. Diastolic arterial pressure rose by a maximum of 11-18%, while pulse pressure rose by 20-26%. Mean dynamic pressure showed virtually no change (±8%). PWV of the aorta slowed down somewhat during the test on P. I. Klimuk but did not change in V. I. Sevast'yanov.

Ejection time and mechanical systole diminished by 10-16% in P. I. Klimuk and 25-23% in V. I. Sevast'yanov. The phase of isovolumetric contraction was 17% longer in the former and showed virtually no change in the latter. The interphase coefficient K [5] increased by 28-30%. In addition to general changes inherent in all tests with LBNP, each of them presented its own distinctions. Apparently, best endurance of LBNP by the commander was observed on the 94th and 67th preflight days. According to hemodynamic indices, optimum endurance was referable to the first test in V. I. Sevast'yanov, and the reaction to the second test was more marked. P. I. Klimuk presented the greatest increment of heart rate, 31-36%, in the LBNP test 8 days before lift-off. There was a more distinct decrease of stroke and minute volumes, by 32-33%. In V. I. Sevast'yanov, at the last test the maximum increase in heart rate constituted 23-30%. Stroke and minute volumes decreased by 32-36% and 8-17%, respectively.

According to the reports of V. I. Sevast'yanov, LBNP was better tolerated in weightlessness than before the flight. P. I. Klimuk did not observe any appreciable difference in weightlessness. According to the results of inflight tests, there were more marked changes in stroke and minute volumes, and peripheral resistance of vessels. The arterial pressure reaction did not differ from the preflight level, and PWV in the aorta increased. There were greater changes in phase structure of the cardiac cycle: 70-80% elevation of interphase index in P. I. Klimuk and 40-50% in V. I. Sevast'yanov. In P. I. Klimuk, stroke volume showed a maximum drop of 50-53% and minute volume, 37-38% (14th-31st day). On the 14th day, we also observed the maximum increase in heart rate, by 40%. The test performed on the 37th day resembled the second preflight test, which was rated as best with regard to endurance. The reaction to LBNP in flight was stable in V. I. Sevast'yanov. The stroke volume dropped to 34-45% and minute volume, to 25-35%, in the tests on the 22d, 31st and 37th days. These changes resembled the results

of the second preflight test, in which there were maximum deviations of most hemodynamic indices.

With LBNP, increment of actual peripheral resistance in V. I. Sevast'yanov constituted 56-38% on the 22d-31st day and only 24% on the 37th day. The LBNP test on the 53d day was performed against the background of a fluid and sodium load. In P. I. Klimuk, the hemodynamic changes resembled the circulatory reaction with LBNP on the 14th day. In V. I. Sevast'yanov, they were about the same as on the 22d and 37th days.

We examined the dynamics of cardiac contractions and phases of the cardiac cycle with LBNP on the 60th and 61st days. These data did not differ appreciably from those obtained at earlier stages of the flight. Postflight LBNP tests were considered more difficult by the cosmonauts than preflight and inflight ones. The first postflight test elicited maximum hemodynamic changes in P. I. Klimuk. During LBNP against the backgrouhd of a high initial pulse rate, pulse pressure dropped by 37-45%, stroke volume, by 45-50% and minute volume, by 35%. Maximum increment constituted 40%. In our opinion, the increased minute volume toward the end of the test, in the presence of tachycardia throughout the test, was an adverse sign. The reaction to LBNP on the 4th and particularly 6th days did not differ essentially from the 1st and 2d preflight tests, which is indicative of rapid recovery of orthostatic stability in P. I. Klimuk (Figure 1).

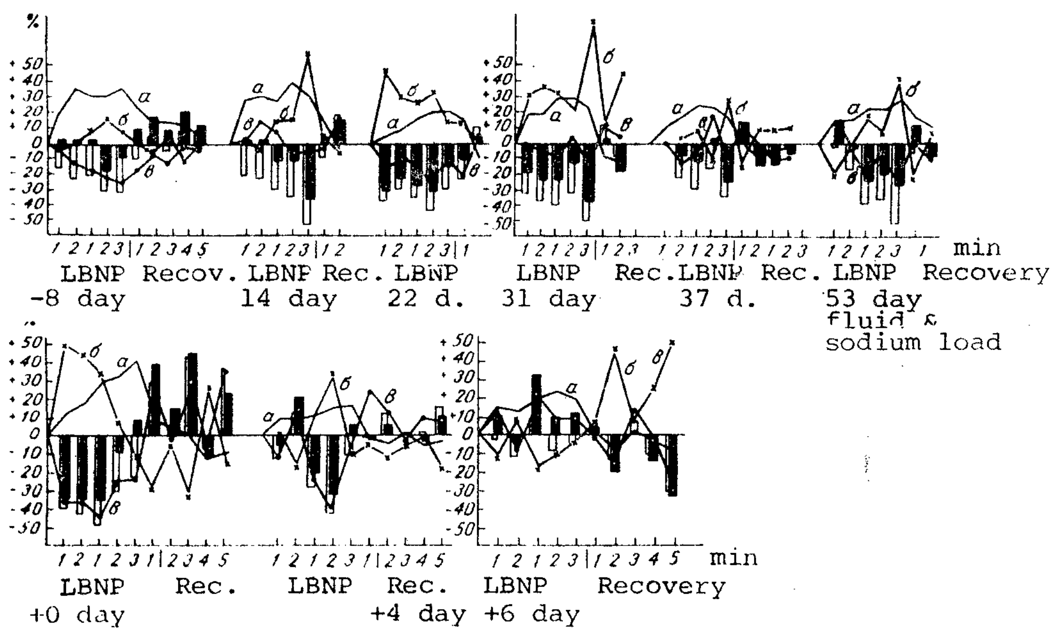

Figure 1. Hemodynamic changes in P. I. Klimuk during LBNP in the preflight period, during mission and postflight period

а) pulse
б) specific actual resistance
в) pulse pressure

white columns--stroke volume
black columns--minute volume

Endurance of LBNP was somewhat better 6 h after the mission in V. I. Sevast'yanov than P. I. Klimu. On the 4th day, the test was associated with the least hemodynamic changes and, apparently, it was the best. On the 6th day, orthostatic stability diminished. The test resembled the second postflight test on P. I. Klimuk; however, a significant decrease of stroke (by 53%) and minute (45%) volumes was noted only in the 1st min of the test; there was less change in the indices thereafter. After equalization of pressure in the [pressure] suit, cardiac output and pulse pressure increased by 38-55% (Figure 2). During the same test, there was a marked change in phases of the cardiac cycle: the interphase index reached 160%.

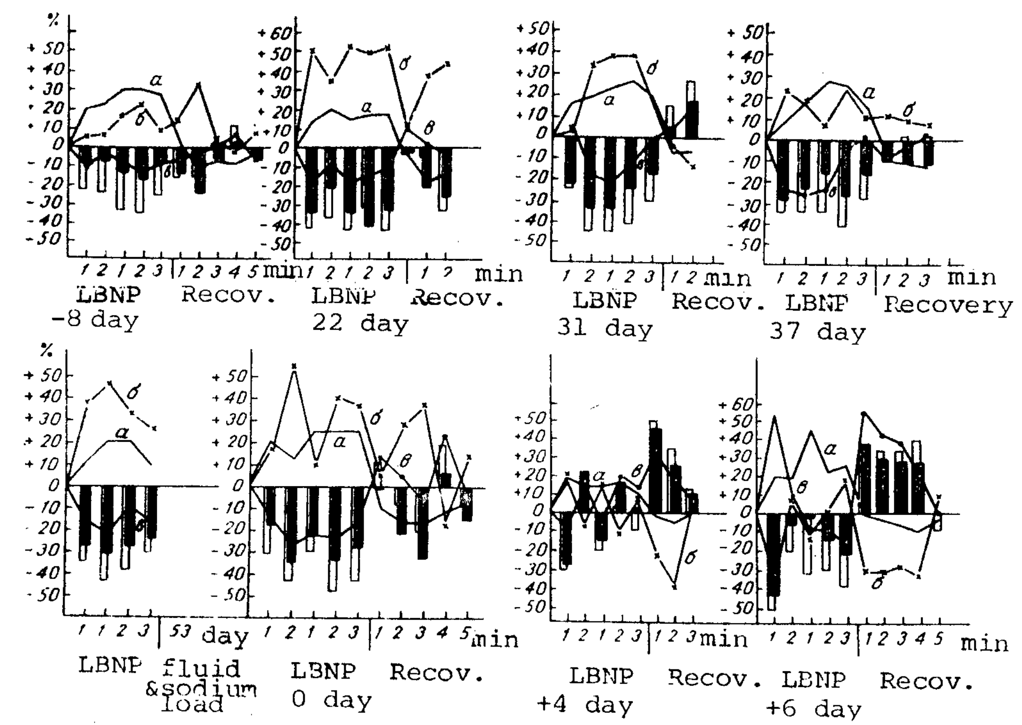

Figure 2. Changes in hemodynamic indices of V. I. Sevast'yanov during LBNP test in the preflight, inflight and postflight periods. Key is the same as for Figure 1.

Thus, the reaction to the functional test with LBNP in weightlessness was in the same direction as on earth with regard to most indices. However, the more significant change in stroke and minute volumes and velocity of pulse wave, as well as duration of phases of cardiac cycle is a sign of diminished orthostatic stability of cosmonauts during the flight. It should be stressed that there was no progressive deterioration of orthostatic stability with increase in duration of the flight.

The reaction to LBNP depends significantly on volume of circulating blood (CBV)[6, 7]. No direct studies of CBV were made during the flight. But,

according to circulatory indices during LBNP, no appreciable differences could be noted between the 14th, 21st and 31st days. Hence, it may be assumed that all of the CBV changes are stabilized sooner, i.e., not later than the 2d week of weightlessness. Nor could we demonstrate a clearcut correlation between filling of jugular veins and blood pressure in them, on the one hand, and reactions to LBNP, on the other. Thus, for the 1st month of the mission, the blood pressure in the jugular veins of V. I. Sevast'yanov was higher than the initial level, and in the 2d month it became the same as the latter, or even lower. Probably, with LBNP in weightlessness, the body retains the capacity to rapidly mobilize deposited blood. As a result, endurance of the test with lowering of central venous pressure remains at a similar level. Apparently, an analogous process takes place during physical training and work.

The choice of LBNP for functional tests is a timely practical question, since it is related to safety of tests during missions.

On the Skylab station and in the preflight and postflight examinations of astronauts on the Apollo program, American researchers [2] used a test with gradual [in steps] lowering of pressure to -50 mm Hg with total duration of 15 min.

There were cases of a presyncopic state among crew members of the first expedition on the Skylab station when the test was performed during the flight, and this served as the reason for limiting pressure drop to -40 mm Hg for a total of 10 min. The system used to lower pressure with LBNP on Salyut orbital stations has not changed since 1974 [1]. It was tested repeatedly in preflight and postflight examinations of the crews of Soyuz-12 and Soyuz-16. There were no instances of worsening of the condition of the cosmonauts. The advantage of less marked pressure lowering is that there is moderate influx of blood to thoracic organs with equalization of pressure in the space. This eliminates, to a significant extent, the danger of appearance of cardiac dysrhythmia and other adverse reactions. After the two expeditions on the Salyut-4 station, there was broadening of opportunity for comparative analysis of informativeness of a wide set of hemodynamic indices and choice of criteria of endurance of the test with LBNP.

Of the recorded circulatory indices, the greatest significance was attributed to dynamics of heart rate, changes in arterial pressure, cardiac output and elastic properties of arteries. Orthostatic endurance was close to the preflight level in P. I. Klimuk on the 37th day and, according to some data (change in phase structure of the cardiac cycle), on the 31st day. On the 37th day, it apparently also improved in V. I. Sevast'yanov. Consequently, signs of normalization of the reaction to redistribution of blood in the lower half of the body were observed toward the end of the 1st or start of the 2d month of the flight.

In the LBNP test 6 h after landing, the changes in output were on the level of maximum values recorded in flight. According to the results of the investigation, it can be concluded that, in weightlessness, with LBNP of 25-35 mm Hg lasting 5 min, acceleration of heart rate could reach 30-40%, decrease in

stroke volume constituted 50-55% and minute volume, 30-37%, with 20-30% increase in velocity of pulse wave in the aorta.

The significance of reorganization of cardiac cycle phases merits re-evaluation. On the ground, a 50% or greater increase in interphase coefficient K, with 35 mm Hg LBNP is prognostically unfavorable.

In weightlessness, during LBNP of 35 mm Hg, other conditions being equal (decreased stroke and minute volumes, faster pulse, etc.), there are more significant changes in phases of isovolumetric contraction and expulsion.

The interphase coefficient could increase by 70%. After landing, everything appears to revert to its place.

There was an appreciable difference in dynamics of recovery of weight and balance of intake and output of fluid between the commander and flight engineer. These indices were better in P. I. Klimuk, and on the 4th-6th day his orthostatic stability was similar to the preflight level. The fluid balance became negative at the end of the 3d day and weight loss constituted 800 g in V. I. Sevast'yanov. By the 6th day, his orthostatic stability worsened again.

Thus, 63-day weightlessness elicits reorganization of extracardiac and intracardiac hemodynamics and worsens the circulatory reaction to LBNP, which should be interpreted as a manifestation of deconditioning of the cardiovascular system and diminished orthostatic stability in the inflight and postflight periods.

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DYNAMICS OF ORTHOSTATIC STABILITY OF COSMONAUTS FOLLOWING 2 TO 63-DAY MISSIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 31-37

[Article by V. V. Kalinichenko, submitted 25 Mar 76]

[Text] It is known that cosmonauts always experience difficulties in re-adaptation to earth's gravitation after space flights, chiefly due to deconditioning of the circulatory system [1-4]. For this reason, it is deemed purposeful to summarize some of the results of studying orthostatic stability (OS)[or endurance] of 25 crew members of Soyuz-4--Soyuz-18 spacecraft [SC] including postflight studies after missions on the Salyut-3 and Salyut-4 orbital stations (OR).

Method

OS was determined 6 and 1 month before the flights. Postflight studies were conducted mainly at the following times: 2-8 h after landing (0 day), after spending the first night on earth (1st day), on the 3d, 7th days, and at later times following longer missions.

We used two variants of orthostatic tests: active vertical position for 6 min and passive position on an orthostatic table, with the head 70° up from the horizontal for 10 min. As a rule, the active orthostatic tests were performed in the morning, when the subjects awakened, and the passive ones 2-3 h after breakfast. Each min of active standing and in even min of passive standing, we recorded and then calculated the following indices by the mechanicardiographic method: heart rate (HR) per min; left ventricular expulsion time; arterial pressure (AP); end systolic pressure (ep); mean dynamic pressure (m); diastolic pressure (d) in mm Hg; arm/leg lateral systolic pressure; pulse wave velocity in vessels of the muscular (Vm) and elastic (Ve) types and ratio between them; stroke index (SI) as the ratio of systolic volume according to Bremser and Ranke to body surface, in ml/m^2. The integral index of orthostatic stability, IIOS, was calculated from the mean values of the above indices and dynamics thereof in orthostatic position [5]. It reflected the degree of adequacy of antigravitation mechanisms and their capacity to compensate for orthostatic perturbance. The ratings

according to IIOS in arbitrary units (arb.u.) corresponded to the following five gradations of OS: 86-100, excellent; 71-85, good; 56-70, satisfactory; 41-55, low and less than 41, poor.

In addition, we determined the cardiac index (CI) as the product of SI and HR, and specific peripheral resistance as ratio of mean dynamic AP to CI.

Results and Discussion

OS was good and excellent in most cosmonauts before the flight, and satisfactory 1 month prior to the flight in only 4 subjects.

Table 1. Dynamics of integral index of orthostatic stability

Number		Duration of flight days	Preflight				Days after flight								Ranking
			6 months		1 month		0		1st		3d		7th		
SS	OR		AOT	POT	AOT	POT	AOT	POT	AOT	POT	AOT	POT	AOT	POT	
12		2	66	65	78	78	42*	—	65	44	79	77	—	—	8
			91	96	93	83	58*	—	82	76	90	84	—	—	3
16		6	—	86	85	88	—	67	87	—	85	92	—	—	1
			—	91	82	75	—	68	70	—	75	80	—	—	2
13		8	81	79	82	73	—	64	70	—	79	71	77	—	5
			—	—	68	68	—	44	42	—	70	60	64	—	11
9		18	—	67	81*	64	24*	—	64	—	68	50	56	48	13
			—	81	79*	65	16*	—	57	—	77	54	24	55	14
14	3	16	88	87	87	92	—	—	81	64	82	67	87	82	6
			72	86	82	90	—	—	69	63	74	82	88	73	7
17	4	30	80	65	65	78	—	47	8	16	67	56	71	64	12
			82	89	78	78	—	61	66	66	82	69	80	79	4
18	4	63	83	81	75	85	—	—	59	70	85	76	76	74	9
			72	74	76	85	—	—	70	70	64	77	72	65	10

Note: The first of each set of two lines refers to data on the commanders and the second, to flight engineers.

AOT) active orthostatic test *) AOT performed in the afternoon
POT) passive orthostatic test

Table 1 illustrates changes in OS only in cosmonauts for whom dynamic determination thereof was made after the flight; it was found to be diminished to some extent or other in all cases. As to ranking of absolute OS levels and extent of decline from the preflight levels, the cosmonauts in whom it was satisfactory 1 month before the mission were ranked as the last four. If we arbitrarily classify orthostatic deconditioning into mild, moderate and marked, expressly these four cosmonauts would be referable to the last category. Thus, this confirms the prognostic significance of initial OS level. Furthermore, it is expedient to adjust preventive measures against deconditioning inflight on an individual basis, with due consideration of preflight OS.

It would be purposeful to consider the degree of orthostatic deconditioning as function of duration of weightlessness separately in cosmonauts who flew on the Soyuz SC and Salyut OR, in view of the fact that conditions and measures for the prevention of deconditioning on Salyut OR were better than on Soyuz SC [6, 7]. According to Table 1, we see that there is a distinct tendency toward increase in orthostatic deconditioning with increase in duration of flights on the Soyuz SC. There was appreciably greater deconditioning of A. N. Nikolayev and V. I. Sevast'yanov after an 18-day flight than after shorter ones.

Orthostatic deconditioning also increased with increase in duration of mission on the Salyut OR. However, this tendency was less marked than after flights on Soyuz SC. Cosmonauts were not much more deconditioned after a 63-day flight on Salyut-4 than after a 16-day flight on Salyut-3. Perhaps the significant difference in orthostatic deconditioning after a 3-day flight was due to individual differences in endurance of the deleterious effect of weightlessness. The sharp decrease of OS in the commander of this crew on the 1st postflight day is not typical for the group under study in these conditions.

Intensification of deconditioning and increased stability of altered regulation of the circulatory system with increase in duration of weightlessness result in slower and incomplete restoration of OS in the first days of re-adaptation following long flights (Figures 1 and 2). This is also confirmed by the rate of recovery of circulation volume in orthostasis. On the day the cosmonauts landed, CI was usually lower than the preflight level, in spite of higher HR. However, circulatory volume rapidly increased under the influence of earth's gravitation after flights lasting up to 16 days, and in 1 day on earth the CI was above the preflight level (Table 2). After a 63-day flight, CI did not reach the preflight level in the same time.

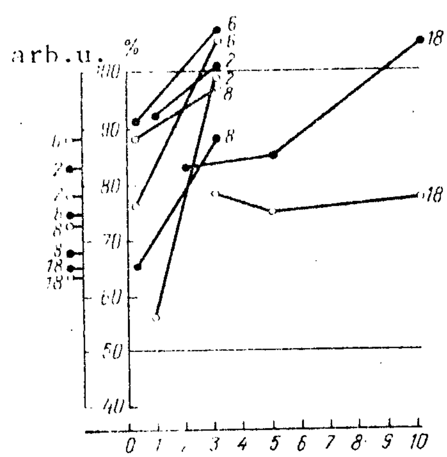

Figure 1.
Change in IIOS in passive orthostatic tests on cosmonauts following missions on Soyuz spacecraft.
X-axis: left scale, absolute value of integral index 1 month before flight; right scale, change in integral index after flight, % of absolute preflight data. The numbers refer to duration of missions; white circles, data for craft commanders; black circles, data for flight engineers

Table 2. Some mean circulatory indices with cosmonauts in orthostatic position following missions, and changes therein, as percentage of preflight data (in parentheses)

Number		Flight duration days	Crew member	Post fl. days	Index						
SC	OR				HR	AP_{es}	AP_d	Ve	SI	CI	AP/CI
12		2	C	0	135 (+105)	108 (—7)	77 (+13)	930 (—7)	9 (—50)	1220 (+3)	75 (—4)
				1	101 (+53)	118 (+2)	86 (+26)	700 (—30)	17 (—6)	1720 (+44)	59 (—24)
			FE	0	102 (+63)	112 (—6)	76 (+19)	940 (+34)	16 (—58)	1630 (—32)	61 (+61)
					77 (+22)	121 (+2)	85 (+33)	780 (+11)	21 (—45)	1620 (—33)	64 (+68)
13		8	C	0	114 (+30)	126 (+7)	88 (+13)	780 (+3)	18 (—5)	2050 (+21)	50 (—5)
				1	102 (+17)	116 (—2)	81 (+4)	690 (—9)	23 (+21)	2370 (+40)	42 (—20)
			FE	0	148 (+68)	112 (—10)	79 (+11)	870 (+1)	11 (—50)	1630 (—16)	55 (+20)
				1	138 (+41)	114 (—8)	81 (+13)	820 (—5)	14 (—35)	1930 (+43)	50 (—22)
14	3	16	C	1	108 (+116)	110 (—13)	72 (—4)	700 (+12)	21 (—34)	2280 (+43)	37 (—35)
			FE	1	103 (+52)	118 (+3)	68 (—10)	800 (—13)	28 (+47)	2900 (+125)	34 (—51)
17	4	30	C	0	120 (+79)	123 (+6)	90 (+17)	900 (0)	9 (—44)	1080 (—8)	93 (+8)
				1	105 (+40)	105 (—10)	67 (—13)	720 (—20)	17 (+6)	1740 (+48)	49 (—43)
			FE	0	91 (+38)	121 (+6)	79 (0)	890 (—5)	11 (—27)	1010 (—2)	94 (+6)
				1	85 (+29)	115 (+1)	77 (—2)	920 (+8)	12 (—20)	1020 (—1)	90 (+1)
18	4	63	C	1	107 (+43)	132 (+7)	97 (+21)	790 (+5)	14 (—39)	1500 (—13)	75 (+34)
			FE	1	98 (+20)	128 (+3)	90 (+22)	810 (—5)	17 (—19)	1670 (—3)	65 (+22)

Key:

C) data for spacecraft commander

FE) data for flight engineer

SC) spacecraft

OR) orbital station

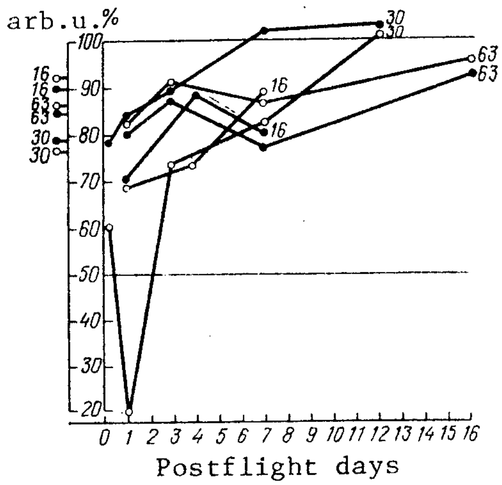

Figure 2.
Same as Figure 1, but following flights in Salyut orbital station

Thus, the studies revealed that there is an increase in orthostatic deconditioning with increase in exposure to weightlessness. However, the rate of increase therein is appreciably lowered by measures to prevent the adverse effects of weightlessness.

At the present time there is no question about the importance of measures to prevent deconditioning. Already after the 2-day flight of A. S. Yeliseyev and Ye. V. Khrunov, which involved passage from one SC to another through open space, it could be considered that their physical activity during the flight aided in good preservation of OS. Thus, 1 day after landing, their OS constituted 105 and 109% of preflight levels. In contrast, the fact that the crew of Soyuz-12 was less active in another 2-day mission was apparently one of the reasons why their OS constituted only 71 and 95% of preflight levels after 1 day back on earth. Evidently, the better system of preventive measures against the deleterious effect of weightlessness on Salyut OR was more effective in counteracting orthostatic deconditioning than during the missions on Soyuz spacecraft. Thus, after a 63-day flight in Salyut-3, the cosmonauts were less deconditioned than after an 18-day mission in Soyuz-9. It is significant that the same flight engineer, V. I. Sevast'yanov, participated in both flights.

In most cases, there was uniform and rather rapid recovery of OS. In these cases, we could refer to adequate preservation of functional reserves of the circulatory system. There was slower recovery of OS in cosmonauts after the 18-day mission on Soyuz-9 and the 63-day one on Salyut-4. These cosmonauts presented a second decrease of OS at the end of the 1st week of readaptation. This suggests overfatigue of regulatory mechanisms of the circulatory system under the influence of earth's gravitation that is perceived by the cosmonauts as hypergravitation after being weightless. Evidently, an excessively active motor regimen played a substantial role following the 18-day mission.

The marked and early secondary decline of OS on the 1st day after a 30-day mission in the commander was probably largely due to inertness of humoral mechanisms of circulatory homeostasis. This assumption is confirmed by the good rate of OS recovery on the next days. In this regard, the rapid OS recovery of cosmonauts after a 30-day mission, as compared to a 63-day flight, merits attention. Perhaps the pharmacological agents with anabolic action given to the cosmonauts after the 30-day flight, but not after the 63-day mission, were beneficial.

It is purposeful to supplement the general description of OS changes with consideration of some special mechanisms of orthostatic reactions. Retention of the capacity to increase arterial tonus is beneficial, according to velocity of pulse wave and peripheral resistance, and in the case of a significant decrease in circulatory volume as, for example, in the cosmonauts after an 18-day flight [8], this mechanism becomes the principal and, apparently, last reserve for compensation of inadequate venous return. The tendency toward decreased arterial tonus and peripheral resistance in orthostasis was only observed in the craft commander on the 1st day after a 30-day flight. For this reason, the still satisfactory circulation volume (CI = 1740 $ml/min/m^2$) was not enough to provide the necessary delivery of blood to vital organs, and the test was interrupted prematurely (see Table 2). The fact that CI rises to above preflight levels in cosmonauts after 1 day on earth following missions lasting up to 30 days could be an indication of increased venous tonus as well. But the slow increase in vascular tonus under the influence of earth's gravitation must be considered the main cause of marked orthostatic instability in the first minutes and hours after landing. Evidently, the problem is to activate it at the final stage of the mission.

Considering that deficient venous return is the chief cause of postflight orthostatic instability, it is interesting to discuss the change in severity of orthostatic tachycardia, with due consideration of active pumping in of blood by the heart [9]. Perhaps, tachycardia in orthostasis is not only an index of intensity of antigravitation mechanisms, but an effective component of the orthostatic reflex. According to data of both American researchers [10] and our own (see Table 2), in orthostasis the HR increases with increase in flight duration to 8 days, reflecting a corresponding decrease of OS. With further increase in duration of flights, there is a tendency toward decrease in orthostatic tachycardia. One could hardly interpret this tendency was a beneficial phenomenon. For example, even with sharp decrease in OS of cosmonauts after an 18-day flight and in the commander after a 30-day flight, HR constituted 120-124 beats/min and was inadequate to supply the required volume of circulation. Thus, with increase in duration of flight, apparently there is an increase in involvement of the cardiac component in lowering OS.

A comparison of changes in endurance of active and passive standing indicates that deconditioning of the vascular component plays a larger part in insufficiency of the venous return. At the same time, the functional capabilities of the muscular pump remain relatively high. Thus, while preflight endurance

of both types of orthostatic loads was virtually the same in the subjects (IIOS 82 arb. u.), endurance of passive standing was poorer than active, with statistical reliability (P = 0.01) after the flight. On this basis, we could recommend exercise, in the form of walking, stepping from one foot to the other, etc., for cosmonauts in order to prevent orthostatic disorders.

Apparently, the postflight change in OS of cosmonauts depends on several factors. The initial level of OS, duration of flight, living conditions in the spacecraft and system of prevention of decondition, as well as readaptation regimen appear to be the most important ones. Other factors, that are difficult to take into consideration, are also significant.

The limited number of observations means that our results are merely preliminary. At the same time, the methods developed to study orthostatic stability may be useful in determining the chief causes of decrease thereof.

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SOME PSYCHONEUROLOGICAL REQUIREMENTS IN ASSESSING INFLIGHT FUNCTIONAL STATE OF COSMONAUTS

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[Article by V. I. Myasnikov, O. V. Kon'kova and F. N. Uskov, submitted 2 Dec 74]

[Text] The neuropsychiatrist who evaluates the current state of cosmonauts during missions has to work under specific conditions. They include the brief communication sessions, limited input of information about the cosmonaut's condition, inevitable interference, limited free verbal exchanges between neuropsychiatrist and cosmonaut, need for operational [immediate] conclusions and recommendations. As a result, the expert may feel that there is a shortage of information, i.e., he may be in a vague situation. This becomes particularly perceptible when he has to establish a similarity between a current state and its initial "level," that is typical for the individual under observation.

Our objective was to demonstrate the distinctive features of assessment of similarity on the basis of incomplete information.

Methods

In selecting methods for our study, we tried to obtain an experimental situation that would reflect, as fully as possible, the dynamic aspect of the process of judging similarity. For this purpose, we referred to synonym dictionaries and consulted linguists to select two series of synonyms, with different mechanisms involved in evaluation of similarity of meaning. The first series of synonyms was: examine, view [inspect], scrutinize, look closely and pore over; similarity of synonyms as to meaning could be determined both on the basis of direct estimation of similarity and use of the discursive approach. The second series of synonyms--negative, denying, disapproving, unflattering, unfavorable-- was less suitable for discursive approach to similarity of meaning than the first one; here, determination of similarity was based on the direct impression. This was indicated by the results of a special experiment we conducted with the participation of 20 people with various (secondary, specialized and higher) levels of education.

After being shown a series of synonyms, they were asked to describe verbally the similarity and difference in meanings of the synonyms in the series. It was found that, regardless of knowledge of language, this problem presented great difficulties for the "negative" series of synonyms, and in some cases could not be done at all. At the same time, the similarity and difference between synonyms in the second series ("examine") could be better described verbally.

The second methodological procedure which, in our opinion, reflects the dynamics of the thinking activity in the process of judging similarity of synonyms, was to use a procedure of one of the psychometric methods, the triad method [1], which made it possible to provide a quantitative expression of the opinions of the subjects about similarity of compared stimuli on the basis of multiple comparison of stimuli in all sorts of combinations.

In this investigation, what was important from the standpoint of dynamics of judgments was also the fact that the experiment was conducted as well in an altered functional state. For this purpose, the subjects took psychopharmacological agents referable to different groups.

Experimental procedure: In accordance with the triad method we used, the synonyms were put in all possible combinations of three, i.e., triads. After keying the synonyms of any series with the letters a, b, c, d, e, we obtain the following combinations: a ^{b} c, b ^{d} e, d ^{a} e, etc. Each triad is presented three times, and the reciprocal position of the stimuli (synonyms) has to be changed. For example, for the triad a ^{b} c we obtain two more: c ^{a} b and b ^{c} a. Thus, we have 30 triads in all. The immediate task for the subject was formulated in the instructions as follows: "You will be shown cards, such as:

keen

precise correct

Your task is to read the top word. Explain its meaning. Then read the other two words and decide which is closest in meaning to the top one. If this applies to the word on the left (precise), place the card to the left, and if it applies to the word on the right (correct), place the card to the right."

In order to increase diversity in the subject's performance, the triads referable to both series were presented in the same test, being shuffled with one another and 36 "ballast triads" in random order. Thus, there was a total of 96 triads; the entire set was presented in two sessions with a 30-min break between them.

Drug experiment: Under controlled conditions (use of placebo) we tested piridrol (4 mg), tisercin (25 mg), and aminazine (25 mg). The drugs were ingested in starch capsules. To assure a more rigid placebo control, the instructions pertaining to the drugs were vague. The subjects began to work with the triads 1 h after intake of the capsule. The procedure for presenting synonyms in the drug series did not differ from the background. In all, we conducted five series of experiments: I) background, II) placebo experiment, III) tisercin, IV) piridrol and V) aminazine.

The main experimental group consisted of 8 men 28-36 years of age who had graduated from a VUZ and worked in the same field.

The results were processed separately for each series of synonyms. In our experiments, the opinions as to similarity of meaning of synonyms were reflected in the results of the choices the subjects made for each triad. On this basis we calculated the index of stability of judgment, i.e., number of times a given subject changed his mind in the drug series, as compared to the background (for the entire set of triads),--ΣQ_{pm} [pm probably refers to Russian words for change of mind]. The reliability of differences in ΣQ_{pm} in different series was determined by using the theorem of Moivre-Laplace with a preset significance level of $P = 0.05$. We processed triads for which at least one subject gave the same opinion in all series.

Results and Discussion

A comparison of ΣQ_{pm} in the placebo series to the ΣQ_{pm} in the drug series revealed no statistically significant differences in compared values. The Table shows that the fluctuations of ΣQ_{pm} from series to series were negligible, both in the first and second series of synonyms. Hence, it could be concluded that changes in functional state do not affect the process of making judgments as to similarity of synonym meanings, since our data show that the ratio of stable and unstable opinions, as compared to the background, remains constant in all series.

At the same time, we were impressed by the high values of ΣQ_{pm} in the second series of synonyms, as compared to the first; this difference was statistically significant in the tests with tisercin.

The obtained facts indicate that, although the opinionsas to similarity of meaning in both series of system are stable, as related to the initial, background level, the actual level of this stability is lower in the "negative" series, and this is apparently related to the nature of judgments made here. Thus, it was shown that opinions made on the basis of immediate impressions, in situations where information is incomplete, are more subject to instability than judgments of a discursive nature. In our experiments, this was manifested because of altered functional state of the subjects.

The demonstrated facts must be taken into consideration in a real situation where a diagnosis is made. In view of the fact that, in the case of operational diagnostics according to incomplete data there is a definitely high share of opinions about similarity according to immediate impressions, such opinions are subject to changes in functional state, and this must be taken into consideration when deciding on the optimum work schedule for an expert in shifts. Individual characteristics of stability of such judgments may also be quite important in the work of an expert neuropsychiatrist. As shown by the data in the Table, the degree of instability of opinions of some subjects according to the immediate impressions about similarity of synonyms may be particularly high (subjects 6 and 7). In all probability, this circumstance is one of the causes of diminished accuracy of these opinions, including verbal formulation of a conclusion by an expert. For this reason,

determination of dissimilarities in synonym meaning could be used as a unique functional test for the expert.

Number of times subjects changed their minds about similarity of synonyms, as compared to background

1st syn.: examine, view, scrutinize, look closely, pore over

Series	Subjects 1	2	3	4	5	6	7	8	ΣQ_{pm}
II	2	12	2	5	5	4	4	5	39
III	1	4	4	6	3	5	3	3	29
IV	5	3	7	5	1	0	5	5	31
V	2	7	6	7	6	3	1	3	35
ΣQ_{pm} for all series	10	26	19	23	15	12	13	16	134

2d syn.: negative, denying, disapproving, unflattering, unfavorable

Series	Subjects 1	2	3	4	5	6	7	8	ΣQ_{pm}
II	3	10	5	7	5	6	11	7	54
III	6	4	5	3	2	7	10	8	45*
IV	5	3	7	9	7	8	4	4	47
V	6	3	4	10	5	8	7	3	46
ΣQ_{pm} for all series	20	20	21	29	19	29*	32*	22	192*

*With P = 0.05 it can be maintained that ΣQ_{pm} of the 2d series of synonyms are greater than those of the 1st series.

On the whole, this study enables us to consider that investigation of the psychological structure of expert activity is a rather productive approach to defining criteria for screening and purposeful training thereof.

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HISTOCHEMICAL STUDY OF DIGESTIVE ORGANS OF RATS FOLLOWING FLIGHT ON KOSMOS-605

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 40-46

[Article by M. G. Shubich, L. L. Goryacheva, V. I. Dudetskiy, N. M. Lutsenko and G. M. Mogil'naya, submitted 25 May 76]

[Text] A comparative study was made of the stomach, small and large intestine, and pancreas of rats that had spent 22.5 days onboard Kosmos-605 satellite, as well as rats from a ground-based model experiment and intact rats maintained on the same diet in a vivarium.

Methods

Material was taken for this study after completion of the flight and ground-based experiments: 8 rats were examined on the 2d postflight day and 5 after the ground-based experiment. There were as many control rats as experimental ones.

Tissue specimens were fixed in Gamperl, Carnoy and Becker mixtures, then imbedded in paraffin. Organ preparations stained with hematoxylin-eosin, picrofuchsin according to van Gieson and methanyl yellow with additional staining of nuclei according to Feulgen were submitted to histological examination. Polysaccharides and glycoproteins, demonstrated by means of a set of histochemical methods, including the PAS method of A. L. Shabadash [1], basic brown stain at pH 1.0 according to M. G. Shubich [2] and alcian blue at a pH of 2.7 according to Mowry [3]. The demonstrated carbohydrates were identified by the system of M. G. Shubich et al. [4]. The set of histochemical methods described by M. G. Shubich et al. [5] was used for demonstration of proteins of pancreatic acinar cells.

A combined ocular grid was used to calculate volumetric proportions of the substances studied according to G. G. Avtandilov [6]. According to the data of this author, the percentage of points coinciding with stained microstructures characterizes the share occupied by the substance in question both in the overall area and overall volume of examined preparations. Lymphoid cells were counted per 0.16 mm^2 square of an ocular grid.

Results and Discussion

The mucosa of the stomach and intestine of experimental rats did not differ essentially from that of control animals with regard to histological structure. Epithelial cover cells were missing from some parts of the mucosa in only a few of the rats in the flight group and model experiment on the 2d day after the tests. Dilatation of blood vessles in the wall of the stomach and intestine was observed in experimental and control rats.

Along with minor edema of the stroma of some villi in their apical region, there was lamination and fragmentation of epithelium of the duodenum of some animals in the model experiment, on the 2d and 27th days after termination thereof. Analogous changes were observed in the jejunum of some control animals and rats in the flight group. It is difficult to relate these changes to the effects of experimental factors since, according to the data of M. A. Vorontsova and L. D. Liozner [7], desquamation of epithelia cells at the apex of intestinal villi of rats and dogs is a normal phenomenon, and it is an expression of the process of physiological regeneration of the epithelium. Vascular dilatation could be the result of sacrificing the animals.

We examined the condition of the lymphoid system of the stomach and intestine by counting lymphoid cells on the surface and deep in the lamina propria of the mucosa. Estimates revealed that the number of lymphoid elements diminished only deep in the gastric mucosa, by 34% as compared to the control ($P<0.05$) on the 2d day after the model experiment. As compared to the control, the number of lymphoid elements in the duodenum and jejunum, in the stroma of the villi, increased by 88% ($P<0.02$) and 110% ($P<0.001$), respectively, and by 140% ($P<0.005$) and 30% ($P<0.02$), as compared to the number of such elements in the flight group of rats. On the 2d postflight day, the number of lymphoid elements in the jejunum increased by 61%, as compared to the control ($P<0.01$). There was a 66% increase in amount of lymphoid elements in the colon of animals in the ground-based experiment, as compared to the control ($P<0.05$).

It is difficult to derive definite conclusions from these data. Perhaps, the observed changes reflect phasic changes in migration of lymphoid cells to areolar connective tissue of the gastrointestinal tract from small blood vessels. We did not visually demonstrate changes in number and morphology of follicles of the walls of the stomach and intestine of intact animals and experimental groups of rats.

In control animals, staining by the PAS method revealed intensive staining of extracellular secretions and apical regions of the cytoplasm of cover cells of the gastric epithelium (Figure 1a). Extracellular secretions presented the most intensive reaction to basic brown. In the lower two-thirds of the gastric cryptae, secretions stained with this dye were demonstrable in the apical part of all epithelial cells. With alcian blue, the extracellular secretion demonstrated an intensive reaction, while the epithelium of the upper third of the gastric cryptae and some cells of the surface epithelium

reacted faintly. A moderate reaction was demonstrated in the epithelium of the lower two-thirds of the gastric fossae (Figure 1b). This warrants the belief that extracellular secretions and secretions of the gastric cover epithelium contain a neutral carbohydrate component, sulfosaccharides and sialosaccharides. Sulfosaccharides were demonstrable in small quantities in the surface epithelium, and sialosaccharides, only in isolated cells.

In fundal cells of the stomach, carbohydrates were present only in the mucocytes of the necks and secretory segment. Both variants of mycocytes were distinctly stained by the PAS method (see Figure 1). The neck mucocytes were also stained with basic brown and alcian blue. A few mucocytes reacted to basic brown and alcian blue in the secretory segment of fundal glands. The obtained data indicate that there are a neutral carbohydrate component, sulfosaccharides and sialosaccharides in mucocytes of the necks and a few mucocytes of the secretory segment. Most mucocytes of the secretory segment of the glands contain only a neutral carbohydrate component. According to morphometric studies, PAS-positive carbohydrates constitute a mean of 66.5% in the epithelium of gastric cryptae.

On the 2d postflight day, the neutral carbohydrate component had disappeared from the cytoplasm of mucocytes in the secretory segment of fundal glands. There was also a sharp decrease of this component in the cytoplasm of cryptal epithelial cells. Some decrease in neutral carbohydrate component was also inherent in the cytoplasm of mucocytes of the necks of fundal glands. Some cells appeared in the surface epithelium, which failed to demonstrate neutral carbohydrates, and the overall amount of these substances diminished (Figure 2a). There was a sharp decrease in sialosaccharide content of extracellular secretions, cytoplasm of cryptal epithelial cells, as well as mucocytes of the neck and secretory segment (Figure 2b). Decreased alcianophilia was associated with a decrease in sulfosaccharide content of surface epithelium of the upper third of the gastric cryptae. According to morphometric studies, PAS-positive substances in the epithelium of the gastric cryptae constituted a mean of 48% on the 2d postflight day, i.e., there were considerably fewer than in the control.

These data are very interesting, since the decreased mucine-producing capacity of gastric epithelial cells inevitably leads to a decline of protective properties of the mucous defense barrier with regard to aggressive components of gastric juice (pepsin, hydrochloric acid). Menguy and Masters [8], Spicer and Sun [9] attribute importance to these factors in development of acute ulcerations of the gastrointestinal tract which, according to Selye [10], is related to a stressor reaction. Lambert et al. [11] believe, on the basis of historadioautographic studies, that depressed synthesis of sulfated glycoporteins in gastric epithelium is the cause of peptic ulcers in rats with immobilization stress. Since it is quite possible that the flight group of rats could develop a stressor reaction, one should consider that the histochemical changes in the epithelial lining of the stomach and other mucine-producing cells are related to stress. The observed histochemical changes are transient, since the carbohydrate content of the microstructures of the gastric mucosa that we studied corresponded on the whole to the control on the 27th postflight day. However, the neutral carbohydrate component was still low in the cell cytoplasm of the lower two-thirds of the cryptal epithelium.

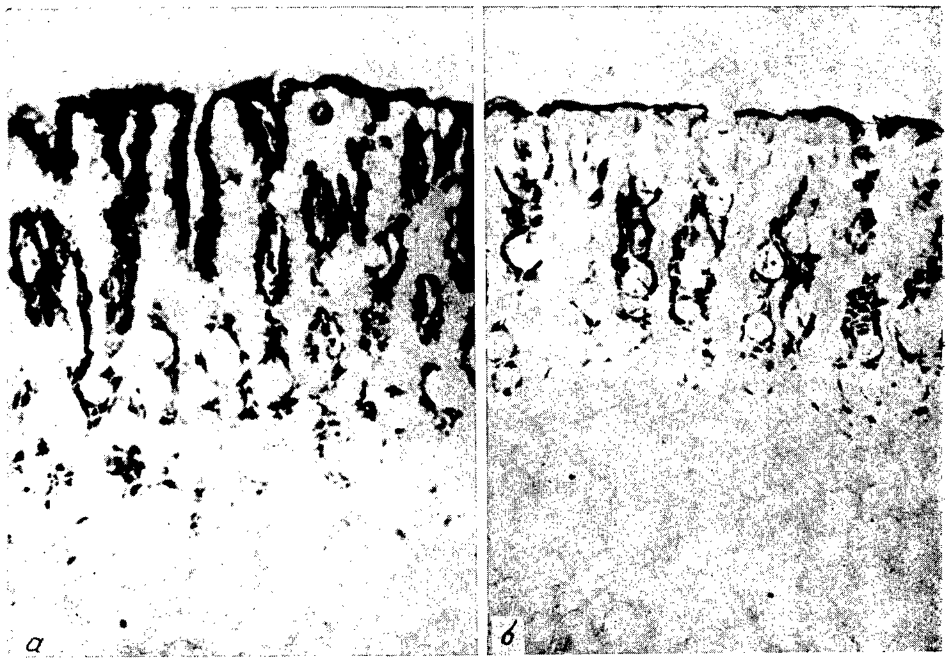

Figure 1. Stomach of rat in control group. Objective 20×; ocular 7×. Explanation given in the text.

a) PAS staining b) alcian blue, pH 2.7

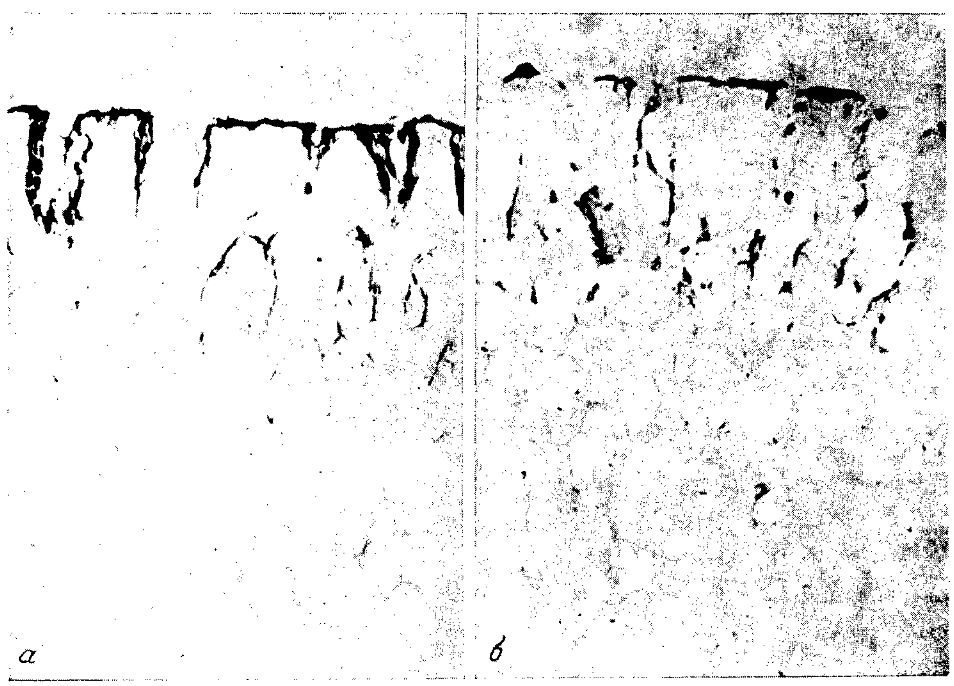

Figure 2. Stomach of rat after flight onboard Kosmos-605 satellite. Objective 20×; ocular 7×. Explanation given in the text.

a) PAS stain b) alcian blue, pH 2.7

Both examinations following the model experiment failed to demonstrate appreciable changes, as compared to the control, in carbohydrate content of epithelial lining of the stomach and secretory cells.

Small intestine and colon: Histochemical study of carbohydrates revealed that there is an increase in sialosaccharide and sulfosaccharide content of goblet cells of the colon on the 2d postflight day. This change, which is more marked in the upper part of the cryptae, could be related to slower extrusion of secretions, due to possible impairment of peristaltic function of the colon. There was either no change or some decrease in the neutral carbohydrate component of goblet cells of the rat colon.

Pancreas: In control animals, after fixing according to Carnoy, acinar cells stained with bromphenol blue, pH 8.2, showed uniform staining of the basal cytoplasm. There is rather intensive staining of nuclear structures: clumps of chromatin, nucleolus and nuclear membrane. Granules of zymogen, some of which appear much lighter, are demonstrable in the apical part. "Protsion" red 2BS, which reacts at pH 5.6 with lysine and histidine residues [11], stains the zymogen granules, structures of the nucleus and basal cytoplasm similarly. With deamination, there is a sharp decrease in intensity of the reaction with "protsion" red. In most of the terminal regions, there is uniform staining of acinal cells with bromphenol blue and "protsion" red.

In view of the information concerning localization of numerous ribosomes in the basal part of the cytoplasm of acinar cells [12], as well as the fact that cation proteins bound with nucleic acids are demonstrable after fixing according to Carnoy, without elimination of the latter [13], it can be considered that bromphenol blue stains the cation protein of ribosomes in the basal part of acinar cells. Staining with this dye of histones of nuclear chromatin and cation protein of the nucleus which, as we know, is the center for ribosome synthesis, is an indirect indication of such a possibility. Apparently bromphenol blue staining of zymogen granules is related to localization in them of enzymatic proteins of trypsin and chymotrypsin, that are basic in nature, with IET [isoelectric point] at pH over 9.0 [14].

On the 2d postflight day, there was loss of uniformity of staining of cation proteins of acinear cells in different terminal regions. Many of the latter showed a decrease in cation protein content. The differences that appeared are probably due to asynchronous synthesis of enzymatic proteins in different acini. On the 27th postflight day, staining of cation protein of acinar cells was more uniform, while overall intensity of the reaction was higher than on the 2d postflight day, being close to the control level. These changes can be related to restoration of biosynthetic activity of acinar cells.

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547.962.9]-06:612.766.2

MUCOPOLYSACCHARIDES AND COLLAGEN OF TISSUES IN HYPOKINETIC RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1977 pp 44-48

[Article by P. P. Potapov, submitted 30 Dec 75]

[Text] Substantial changes have been demonstrated in fluid-electrolyte metabolism of cosmonauts in weightlessness and in subjects kept on strict bed rest [1, 2]. These disturbances are related primarily to elimination of the hydrostatic component of blood pressure and redistribution of circulating blood mass [3-5]. Investigation of metabolism of mucopolysaccharides involved in binding and transport of fluid and inorganic ions in tissues could demonstrate a number of new factors involved in impairing fluid and electrolyte metabolism in the presence of hypokinesia. It has also been established that acid glucosaminoglycans may have a substantial effect on the properties of collagen structures [5]. There is rather sparse and scattered information about the condition of connective tissue in the presence of hypokinesia [6-8], and it deals primarily with connective tissue elements of skeletal muscles. We found no data in the available literature about the influence of limited mobility on mucopolysaccharide metabolism.

Our objective was to study the collagen and mucopolysaccharide content of animal tissues at different stages of hypokinesia and in the recovery period.

Methods

The study was conducted on 98 white rats (40 of which served as a control) weighing 180-220 g. The control group was kept in the usual vivarium cages. Experimental animals were put in individual small cages made of plexiglas to restrict mobility. All of the animals were kept in the same room and fed a complete diet with water ad lib. The rats were decapitated on the 15th, 30th, 60th and 90th experimental days and on the 15th, 30th and 60th days of the recovery period following 90-day hypokinesia. Control animals were sacrificed and examined concurrently with experimental ones. In view of the fact that different batches of rats were used in the "hypodynamia" and "recovery period" series, there was a separate control for each series.

Blood serum, tissues of the liver, heart, kidneys, brain and skeletal muscles from the posterior group of the thigh served as the material to be studied. Wet tissue was ground in a mortar and treated successively with acetone and an ether-acetone mixture (3:1) for 1 hour at 37°, according to the recommendations of Mier and Wood [9]. We assayed hydroxyproline by the method of Neuman and Logan [10], hexuronic acids by the method of Dische [11] and hexosamines according to Elson and Morgan [12], in the modification of Gatt and Berman [13], in dry acetone power hydrolysates of tissues. We used the same method to assay blood serum hexosamines.

Results and Discussion

Hydroxyproline, hexosamine and hexuronic acid levels in tissues of control animals remained constant throughout the experiment, so that we were able to combine control data covering 15-90 days.

Restricted mobility led to a significant increase (39.6%) in hydroxyproline content of skeletal muscle tissue as early as the 15th experimental day, and by the 90th day the increment constituted 48.3% (Table 1). On the 15th day of the recovery period there was some decline of muscle hydroxyproline, but the level thereof was 8.7% higher than in the control ($P<0.01$), and it remained almost constant thereafter to the end of the experiment.

Table 1. Hydroxyprolline content of rat tissues (mg/100 g dry defatted tissue) during hypokinesia and in the recovery period

Organ	Index	Hypokinesia: control	15 days	30 days	60 days	90 days	Recovery period: control	15 days	30 days	60 days
Skeletal muscle	M	226,1	315,7	309,0	334,8	335,4	324,4	352,6	351,0	350,2
	±m	5,0	8,5	9,7	8,7	7,7	1,7	9,5	11,8	13,8
	n	25	9	8	8	8	15	8	8	9
	P		<0,01	<0,01	<0,01	<0,01		<0,01	<0,05	>0,05
Liver	M	192,4	192,5	195,6	195,6	191,5	195,5	184,8	180,0	201,8
	±m	2,0	2,3	2,8	2,4	3,1	2,5	5,4	4,0	4,1
	n	20	9	8	8	8	15	8	8	9
	P		>0,9	>0,3	>0,3	>0,8		>0,05	<0,01	>0,2
Heart	M	360,6	359,5	360,7	376,0	388,0	343,5	344,0	354,0	341,5
	±m	3,2	5,1	5,9	6,4	6,1	4,0	6,7	6,7	5,0
	n	20	9	8	8	8	15	8	8	9
	P		>0,8	>0,9	<0,05	<0,01		>0,9	>0,10	>0,7
Kidneys	M	534,7	533,3	538,4	590,4	582,8	492,2	464,4	483,6	489,5
	±m	4,9	13,1	4,5	15,5	12,0	4,5	6,5	7,9	7,9
	n	20	9	8	8	8	15	8	8	9
	P		>0,9	>0,5	<0,01	<0,01		<0,01	>0,3	>0,7

Collagen content, assayed according to hydroxyproline, increased reliably on the 60th and 90th days of hypokinesia, in the heart (by 4.2 and 7.6%, respectively) and in the kidney (10.4 and 9.0%). Hydroxyproline level of

the liver did not differ from the control at all stages of hypokinesia. The change to normal motor activity led to some decline of hydroxyproline levels in the liver and kidneys.

Hexosamine content (Table 2) was low in skeletal muscle on the 15th, 30th and 90th days, in the heart on the 30th day, and in the brain on the 60th day of the experiment. A decline in the liver was demonstrated at all stages of hypokinesia, and it was the most marked (23.0%) after 30 days. On the 60th day of restricted mobility, there was an increase in hexosamines of the heart and skeletal muscle (by 12.6 and 8.9%, respectively), and the tendency toward increase persisted up to the 90th experimental day in the heart. There was little change in hexosamine content of the kidney during hypokinesia.

Table 2. Hexosamine and hexuronic acid content of tissues (mg/100 g dry defatted tissue) during hypokinesia and in the recovery period

	Organ	Index	Hypokinesia					Recovery period			
			control	15 days	30 days	60 days	90 days	control	15 days	30 days	60 days
Hexosamines	Skeletal muscle	M	236,0	215,7	213,8	257,0	189,8	249,0	207,0	211,5	285,8
		$\pm m$	5,4	5,3	4,7	9,0	10,4	4,0	7,5	8,5	7,5
		n	25	9	8	8	8	15	8	8	9
		P		<0,01	<0,01	<0,05	<0,01		<0,01	<0,01	<0,01
	Liver	M	492,6	402,0	379,5	411,8	422,3	518,5	552,0	543,0	523,3
		$\pm m$	9,8	10,0	10,3	11,2	11,4	9,4	11,2	10,6	9,4
		n	21	9	8	8	8	15	8	8	9
		P		<0,01	<0,01	<0,01	<0,01		<0,05	>0,1	>0,7
	Heart	M	384,2	380,8	349,7	432,9	407,5	469,9	381,6	448,2	448,9
		$\pm m$	10,4	8,4	9,1	17,4	16,1	10,2	6,9	10,1	12,1
		n	18	9	8	8	8	15	8	8	9
		P		>0,8	<0,02	<0,02	>0,2		<0,01	>0,1	>0,2
	Kidney	M	1019,4	994,7	1027,5	1032,0	946,5	1202,4	1201,5	1192,5	1161,3
		$\pm m$	11,4	13,0	17,6	17,0	36,9	19,9	29,7	25,4	24,2
		n	20	9	8	8	8	15	8	8	9
		P		>0,1	>0,7	>0,5	>0,05		>0,9	>0,7	>0,1
	Brain	M	1456,2	1406,7	1496,3	1387,5	1340,6	1443,3	1449,4	1458,7	1433,3
		$\pm m$	22,1	29,6	41,8	13,6	36,3	16,4	13,5	33,3	21,8
		n	25	9	8	8	8	18	8	8	9
		P		>0,1	>0,4	<0,01	<0,01		>0,7	>0,6	0,7
Hexuronic acids	Skeletal muscle	M	63,2	60,7	71,0	66,4	68,1	70,2	126,8	92,1	71,8
		$\pm m$	0,7	±1,8	1,9	1,2	1,5	2,2	±2,7	6,1	±2,2
		n	25	9	8	8	8	15	8	8	9
		P		>0,1	<0,01	<0,05	<0,01		<0,01	0,01	>0,5
	Heart	M	157,9	166,0	149,8	137,3	141,0	170,4	186,0	159,0	221,8
		$\pm m$	4,1	7,8	6,3	11,1	16,6	1,6	5,9	8,5	16,1
		n	20	9	8	8	8	15	8	8	9
		P		>0,3	>0,2	>0,05	>0,4		<0,02	>0,1	<0,01
	Kidney	M	202,8	226,4	223,8	239,5	233,8	192,8	207,5	213,3	191,5
		$\pm m$	4,9	9,9	13,2	9,7	13,3	3,6	7,4	11,8	7,1
		n	18	9	8	8	8	15	8	8	9
		P		<0,05	<0,05	<0,01	<0,05		>0,05	>0,1	>0,8
	Brain	M	306,6	251,6	327,8	259,4	307,5	286,1	332,6	302,5	269,4
		$\pm m$	5,5	11,2	13,3	7,6	5,1	10,7	12,3	20,5	6,5
		n	22	9	8	8	8	15	8	8	9
		P		<0,01	>0,1	<0,01	>0,6		<0,01	>0,4	>0,1

The hexosamine level in the rats' blood serum was low, as compared to the control, on the 30th and 60th experimental days (8.3 and 12.9% decline, respectively) and rose toward the end of hypokinesia (90th day) by 7.2% (in all cases, $P<0.05$).

With the change to normal motor activity, there was rapid normalization of hexosamine content of kidney and brain tissues. In the recovery period, the hexosamine level remained quite low in skeletal muscle to the 30th day; however, by the 60th day the levels thereof increased by 14.8%. On the 15th day of the recovery period, there was a 6.5% rise in hexosamine levels of the liver and 18.9% drop in the heart; after 60 days of normal motor activity there was normalization of hexosamine levels in these organs.

We failed to observe a parallel in dynamics of changes in hexosamine and hexuronic acid content of tissues. This is indicative of impaired balance of acid and neutral mucopolysaccharides in them.

On the 30th, 60th and 90th experimental days there was a 12.3%, 5.1% and 7.8% elevation, respectively, of hexuronic acid levels (see Table 2) in skeletal muscle; a rise was observed throughout hypokinesia in the kidneys. There was a 17.1 and 14.6% decline ($P<0.01$) of level of acid mucopolysaccharides on the 15th and 60th experimental days, respectively; a tendency toward decrease was also observed in the heart, particularly at the late stages of hypokinesia; however, statistical processing revealed that these changes were unreliable ($0.1>P>0.05$).

Hexuronic acid levels were high in all tested tissues on the 15th day of the recovery period. This index reverted to normal in skeletal muscle, kidney and brain 60 days after returning to normal motor activity. On the 30th day of the recovery period, there was a tendency toward decline of acid mucopolysaccharide levels in the heart, and significant accumulation thereof was again observed on the 60th day.

During hypokinesia, there was a decrease in efficiency of tissular respiration due to separation of oxidation and phosphorylation [4]. This leads to activation of glycolysis [15], which is also indicated by accumulation of lactic acid in tissues [16]. Under these conditions, phosphoric ethers of hexoses, which are the immediate precursors of structural components of mucopolysaccharides [17], are used essentialy to meet the energy requirements of the organism, and less are used for synthesis of hexosamines and hexuronic acids. The decrease in hexosamines demonstrated in tissues of the liver, skeletal muscle and heart (at the early stages of hypokinesia) may be attributed to a relative shortage of phosphoric ethers of hexoses. By the 60th day, there is some normalization of processes of synthesis of hexosamines in skeletal muscle and the heart. Under these conditions, the increase in acid mucopolysaccharides of skeletal muscle apparently lags behind the requirements of connective tissue developing in it. The system of synthesis of acid mucopolysaccharides is significantly activated, and it does not immediately readjust to a new level of metabolism in the recovery period. This is the cause of significant increment of hexuronic acids in muscles on the 15th day of the recovery period.

The return to normal motor activity following prolonged hypokinesia constituted another extreme factor [18, 19] against a pathological background and depletion of adaptational and regulatory capabilities of the organism. In the recovery period, the changes in mucopolysaccharide levels of skeletal muscle, liver, heart and brain were more marked, in a number of cases, than during hypokinesia, which is indicative of profound disturbances of regulation of mucopolysaccharide synthesis, both during restricted motor activity and with subsequent change to normal living conditions. The observed changes, which lead to impairment of optimum correlations in connective tissue, could alter tissular permeability and cause redistribution of fluid and electrolytes in the cell-intercellular substance system [2]. Changes in mucopolysaccharide content of renal tissue could have a particularly substantial effect on fluid and electrolyte metabolism. Pathological changes in connective tissue structures of skeletal muscles, which develop during hypokinesia, could have an adverse effect on recovery of muscle function after returning to the usual motor regimen [4].

The obtained data are indicative of the need for a comprehensive study of mucopolysaccharide metabolism during hypokinesia, in order to subsequently consider the desirability of using inhibitors of hyaluronidase, ascorbic acid and rutin for preventive purposes.

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CARDIOVASCULAR REACTIONS TO ORTHOSTATIC TESTS AND HUMAN RESISTANCE TO VESTIBULAR STIMULI

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 48-52

[Article by B. I. Polyakov, B. Ye. Petrenko, A. B. Savvin, I. G. Tazetdinov and A. M. Tarko, submitted 25 Feb 75]

[Text] It is a known fact that there are wide individual differences between people with regard to degree of predisposition to sea sickness (motion sickness). However, expressly which clinical and physiological distinctions determine susceptibility (or, on the contrary, resistance) of man to motion sickness are not yet clear enough.

As far back as 1937 [7], the opinion was voiced that "weakening of functional capability of the cardiovascular system and lack of conditioning thereof" is inherent in individuals with a tendency toward sea sickness. This was also consistent with the findings of M. N. Farfel' [9], who observed that there is greater increase of heart rate and elevation of arterial pressure during the orthostatic test in individuals with more marked vegetative vestibular reactions. Castagliulo and Aurucci [10] found a link between the results of vestibular tests and the test with the tilting table. It consisted of the fact that 6 out of 10 subjects with vestibular hyperreflexia showed reactions on the tilted table that bordered on pathological ones. In recent years, it has also been noted [2, 6, 8] that individuals with low orthostatic stability had a poorer tolerance of vestibular stimuli in a number of instances.

These data led us to raise the question of using cardiovascular indices to predict man's resistance to vestibular stimuli.

Methods

Our methodological approach was based on the following considerations: The organism responds to any stimulus [factor] by altering a number of physiological functions and choosing an optimum mode of vital functions under the altered conditions. And the nature of transient processes reflects the distinctions of the corresponding regulatory mechanisms, so that it can serve as a criterion of their quality [11, 12, 13].

We conducted two series of studies. In the first, we studied the correlation between level of vestibular stability (LVS) and nature of transient processes in the cardiovascular system during the passive orthostatic test (OTp); in the second, we studied the analogous correlation to the active orthostatic test (OTa). The studies were conducted on healthy male volunteers of other than flying occupations: there were 17 men 18-37 years of age in the 1st series and 45 in the same age group in the 2d series.

For the OTp, the tilt table with the subject was changed to close to vertical position (85° angle) for 1-2 s after the subject had stayed in horizontal position for 10-15 min. We continued the observation for another 10-15 min. We recorded the following continuously: cardiointervalogram (CIG), rheovasogram of the legs (RVG) and rheoencephalogram (REG). In analyzing the dynamics of CIG changes, we considered the following parameters: 1) duration of transient process (in min); 2) depth of transient process (in s); 3) fluctuation index (ratio of variance of duration of RR intervals of the EKG in orthostatic position to the analogous parameter in supine position); 5) variance of RR in supine position (in s); 6) error of mean value of RR in supine position (in s); 7) mean value of RR in orthostatic position (in s); 8) variance thereof (in s); 9) error thereof (in s); 10) quadratic area of regulation (in cm^2, calculated by the method of geometric integration).

In analyzing changes in RVG and REG, we estimated the following: 11) electric resistance of tissues of the legs in supine position (in ohms); 12) the same in orthostatic position; 13) change in parameter 12 in relation to 11 (%); 14) vascular reaction time (in min); 15) RVG wave lag time, in relation to the Q wave of the EKG in supine position (s); 16) the same in orthostatic position (s); 17) difference between parameters 15 and 16; 18) change in amplitude of REG in orthostatic position, as compared to amplitude in supine position (%); 19, 20) REG wave lag time in supine and erect positions (by analogy to parameters 15 and 16); 21) difference between parameters 19 and 20.

We usually conducted the OTp test 1 day before the test with motion sickness.

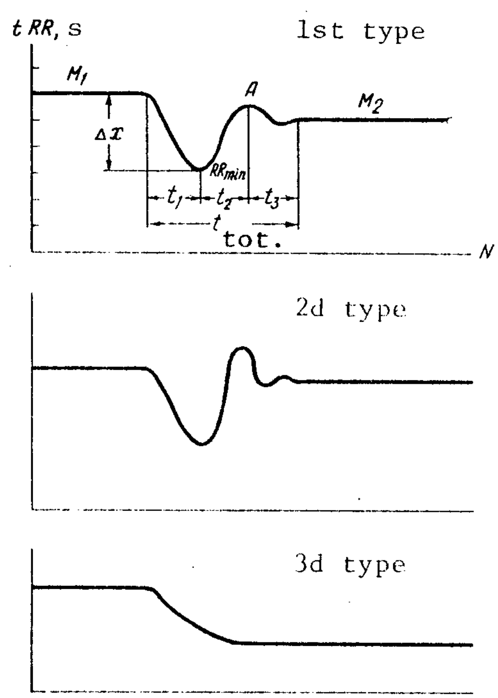
For the OTa, the subject, after lying immobile for 10 min, stood up at the command of the experimenter in 1-2 s and remained standing for 2 min. The EKG was taken continuously, starting in the 8th min of supine position to the end of the test. The following parameters were evaluated in analyzing the transient process (see Figure): 1) mean duration of RR interval in supine position, M_1 (in s); 2) standard deviation of RR interval in supine position (s); 3) minimum value of RR in erect position (RR_{min}); 4) difference between first and third indices (Δx); 5) mean value of RR in erect position after stabilization of pulse (M_2); 6) standard deviation of RR in erect position; 7) difference between indices 1 and 5 (Δy); 8) maximum value of RR while standing before stabilization of pulse (A); 9) duration of phase of acceleration to maximum pulse rate while changing body position (in s, t_1); 10) time between maximum acceleration to maximum slowing of pulse while standing (s, t_2); 11) duration of stabilization phase (from time of maximum slowing to stabilization of rhythm (s, t_3); 12) total duration of transient process, from the moment the subject stood up to stabilization of rhythm (s, t_{tot}); 13) difference between standard deviations in supine and erect

positions; 14) difference between indices 1 and 8; 15) type of transient process (see below); 16) length of envelope of curve on transient process graph (cm); 17) area of regulation (cm^2).

We distinguished the following types of transient processes: 1) acceleration of heart rate and gradual, undulant stabilization on a new level (see Figure); 2) acceleration of heart rate followed by a period of overregulation, when the cardiac intervals are longer during the period of slowing than originally; 3) relatively slow acceleration of rhythm with establishment of a new level immediately, without slowing phases.

The OTa was conducted 30 min before the test with sea sickness.

The LVS was evaluated according to tolerance of rotating test with accumulation of Coriolis accelerations (ACA) by the method of I. I. Bryanov [3]. The test was continued until the subjects developed 2d-3d grade vegetative reactions according to the classification used in special ear, nose and throat expertise, but not over 15 min. The subject's verbal report on his well-being (sensation of discomfort, nausea, etc.) during rotation was supplemented by the results of clinical observation (pallor, hyperhydrosis, overall appearance and behavior) and readings of pulse rate and rhythm, arterial pressure, skin temperature and external respiration parameters. LVS was expressed in minutes of endurance of this test. We examined the relationship between vestibular stability and nature of cardiovascular reactions to the orthostatic tests by means of correlation and regression analysis.



Parameters of transient process during active orthostatic test (explained in the text)

Results and Discussion

A study of paired linear correlation between the above parameters, during OTp, and LVS revealed that none of the coefficients was significant, with confidence coefficient of $P = 0.93$.

Upon further mathematical analysis, we tested multiple correlation between different groups of parameters from the initial set for OTp and LVS in order to single out groups of parameters that would yield the maximum confidence coefficient of difference of the corresponding multiple correlation coefficient (R) from zero. In order to solve this problem, we prepared a special program that expresses the method of gradient decline in the space of groups of parameters. Equations of linear multiple regression were devised with regard to the demonstrated groups of parameters, which expressed the link between LVS and parameters contained in the group, and we evaluated the mean-square errors.

The Table lists the coefficients of multiple correlation and regression for the corresponding parametersin relation to the sought parameter, for all groups distinguished, confidence coefficients and estimation of mean-square errors. As can be seen in the Table, there is a substantial correlation between some groups of parameters of the transient process and LVS during the OTp. The sixth group of parameters presented the highest coefficient of multiple correlation with LVS and the highest confidence coefficient. Thus the optimum model of link between parameters of the reaction to the passive orthostatic test and LVS (model 6) can be expressed in the following equation:

$$Y = -52.8-19.9\cdot X_2+32.4\cdot X_4-3701\cdot X_5-421\cdot X_6-87.6\cdot X_{11}+195\cdot X_{12}-0.763\cdot X_{13},$$

where Y is the sought variable (LVS endurance of test, min); X_2, X_4, ..., X_{13} are the corresponding OTp parameters. The mean-square error of the model equals 2.06 min.

In view of the result obtained, it was deemed purposeful to further search for parameters of the initial state that could be measured more readily and less complex functional tests. For this reason, we conducted a second series of observations, with OTa and evaluation of the transient process only according to heart rate. Analysis of the data with estimation of linear correlations revealed that the corresponding coefficients for parameters of the transient process during the OTa and LVS were not statistically significant ($P = 0.9$). At the same time, investigation of the optimal multiple regression enabled us to obtain a model of the following appearance:

$$Y = 5.14+318.9\cdot Z_2-397.7\cdot Z_6+0.259\cdot Z_{10}-0.253\cdot Z_{12}-350\cdot Z_{13}-4.34\cdot Z_{15}+2.71\cdot Z_{17},$$

where Y is the sought variable, while Z_2, Z_6, ..., Z_{17} are the corresponding parameters of the OTa. The mean-square error of the model equals 4.78 min ($P = 0.93$).

Optimum multiple regression coefficients for OTp

Model No	OTp parameter										a_0	Mean-square error	R	P
	2	4	5	6	11	12	13	15	17	21				
1		15,9		—313						—58	—4,22	3,34	0,709	0,967
2	14,1		—2917								5,29	4,07	0,451	0,772
3					—72,6	152	—597	—49,8			—11,9	4,17	0,540	0,610
4									70,6		5,76	4,23	0,272	0,691
5		21,9		—461				56,1		—64,1	—22,5	3,06	0,787	0,978
6		32,4	—3701	—421	—87,7	195	—0,763				—52,8	2,06	0,935	0,996
7		17,9		—288							—7,1	3,51	0,637	0,966

Note: a_0 is free term of the model.

The obtained data confirmed the existing opinion that there is a relationship between distinctions of reactions to orthostatic tests characterizing the initial state of the cardiovascular system and vestibular stability of man. The mathematical description of this relationship, which we are the first to submit, in the form of equations of multiple regression opens up the possibility of making practical use of this fact to predict vestibular stability depending on the condition of the cardiovascular system.

A comparison of models for active and passive orthostatic tests shows that the latter included parameters characterizing not only the cardiac, but vascular component of the orthostatic reaction (parameters 11-13). It could have been concluded that expressly for this reason the use of this model permits more accurate prediction of vestibular stability than the models for OTa. This is also indicated by the insufficient accuracy of models 2 and 7, in which parameters characterizing only the cardiac component are represented. This assumption appears plausible, if we consider the appreciable role of vascular tonus in regulation, both in the case of orthostatic and vestibular stimuli [4, 5].

However, on the other hand, the lower multiple correlation coefficient and low confidence coefficient for model 3, which contained the same parameters 11-13 (as well as parameter 15) but not a single parameter characterizing the cardiac component of the orthostatic reaction (as in the case of model 4), indicates that it is not the vascular component per se that is prognostically important, but a specific correlation thereof with the cardiac component. There is also a high degree of coordination of activity of various functional elements of the cardiovascular system, in which the principle of systems organization of functions is implemented [1] and thanks to which the aggregate adaptational effect is obtained. In particular, this is manifested by maintenance of adequate correlations between changes in minute volume and peripheral resistance, in spite of the adverse conditions under which the cardiovascular system functions. Thus, the level of systematism (degree of coordination of different branches) is apparently the prognostically most important element, when dealing with the significance of initial state

of the cardiovascular system in reactions to vestibular stimuli. Probably, this is why models 1, 5 and 6, which include parameters referable both to the cardiac and vascular components, have the highest multiple correlation coefficients and lower error factor.

The model for OTa did not include parameters characterizing the vascular component. Perhaps this explains why it is less accurate than the model for OTp.

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DYNAMIC CONTROL OF PARAMETERS OF SPACECRAFT ATMOSPHERE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 53-58

[Article by I. S. Breslav and V. N. Salazkin, submitted 5 Mar 76]

[Text] With increase in duration of space flights and range of work performed by astronauts, it is growing increasingly important to test the hypotheses expounded long ago concerning the possibility of using a nonstationary atmosphere in spacecraft (SC) [1, 4, 10]. In this regard, the problem of implementing dynamic control of atmosphere parameters in such craft ["apparatus"] can be posed.

There are two possible approaches to this problem: 1) "slow" programmed change and stabilization of atmospheric parameters over considerable periods of time to prevent the consequences of the deleterious influence of space factors on the organism; 2) "rapid" control of environment parameters, based on operational monitoring of body functions, the objective of which is to provide a high level of cosmonaut efficiency with different load levels and counteract disturbances of physiological conditions in the case of abrupt changes in state and conditions of vital functions. In this work, we shall touch upon some aspects of substantiating expressly this approach. The main purpose was to determine the patterns of control of partial pressures of oxygen (PO_2) and carbon dioxide (PCO_2) in the SC atmosphere.

Let us first discuss the problem of dynamic, operational control of PO_2.

In order to define the required patterns of PO_2 control, we must first provide mathematical formulation of the general relations between indices of physiological functions to PO_2 and physical load levels, as the main input effect [disturbance] on the organism. The results of many experimental studies must be summarized in order to construct such a model. We used the data referable to the research in [9], as the first step toward developing the model; in this study, the authors investigated the established reactions of man to physical loads varying in force while breathing oxygen and nitrogen mixtures with PO_2 ranging from 85 to 250 mm Hg. Experiments were conducted on four subjects. We considered the following parameters: oxygen uptake ($\dot{V}O_2$, liters/min), oxygenation of arterial blood (SO_2, %), respiratory minute volume (MV, liters),

circulatory minute volume (CMV, liters), rate of cardiac contractions (HR, beats/min), as well as arteriovenous difference for oxygen (AVO_2, ml/liter) and oxygen utilization coefficient (CUO_2, ml/liter).

Identification of the relationships was made using the method of multiple regression [3]. We found the following functions for the physiological static parameters of the human body in question as related to oxygen uptake (as the most adequate index of load level) and ambient PO_2:

$$SO_2 = 27,5 - 1,02\dot{V}O_2 + 0,69PO_2 - 0,0016PO_2^2 \quad (\sigma = 4,0 \ R = 0,91), \tag{1}$$

$$MV = 48,2 + 31,1\dot{V}O_2 - 0,62PO_2 - 0,096\dot{V}O_2PO_2 + 5,62\dot{V}O_2^2 + 0,0019PO_2^2$$
$$(\sigma = 10,1, \ R = 0,95), \tag{2}$$

$$CMV = 21,6 + 13,5\dot{V}O_2 - 0,21PO_2 - 0,014\dot{V}O_2PO_2 - 0,91\dot{V}O_2^2 + 0,0006PO_2^2$$
$$(\sigma = 1,6, \ R = 0,97), \tag{3}$$

$$HR = 129,1 + 63,7\dot{V}O_2 - 0,97PO_2 - 5,85\dot{V}O_2^2 + 0,0024PO_2^2 \quad (\sigma = 7,7, \ R = 0,97), \tag{4}$$

$$AVO_2 = -19,8 + 20,4\dot{V}O_2 + 0,79PO_2 + 0,054\dot{V}O_2PO_2 - 2,83\dot{V}O_2^2 - 0,0022PO_2^2$$
$$(\sigma = 6,7, \ R = 0,94), \tag{5}$$

$$CUO_2 = 4,5 + 0,29\dot{V}O_2 + 0,37PO_2 + 0,018\dot{V}O_2PO_2 - 1,7\dot{V}O_2^2 - 0,00095PO_2^2$$
$$(\sigma = 4,3, \ R = 0,78), \tag{6}$$

where σ is standard [mean-square] deviation; R is the coefficient of multiple correlation. Figure 1 illustrates the graphs of these functions for a series of values of $\dot{V}O_2$ and PO_2.

The model equations and graphs indicate that there is linear decrease (by about 1% per liter $\dot{V}O_2$, [1]) in oxygenation of arterial blood with increase in load, while the reactions of other parameters of the oxygen transport system over the tested range of PO_2 present extremums that depend on $\dot{V}O_2$. As we see, the parameter extremums correspond to optimality conditions, i.e., conditions of minimum tension of physiological systems: minimal MV, CMV and HR levels and maximum values for indices of efficiency of oxygen transport, CUO_2 and AVO_2. Thus, the model demonstrates that it is possible to optimize physiological reactions by altering ambient PO_2. The corresponding patterns of physiologically optimum PO_2 control (static) for each parameter can be determined by using the model of extremum conditions:

$$\partial Fi(\dot{V}O_2, PO_2)/\partial PO_2 = 0, \tag{7}$$

where $Fi(\dot{V}O_2, PO_2)$ is the model equation for a given ith index.

It was found that to optimize the physiological parameters of the organism the following laws of control of respiratory environment PO_2 must apply:

$$PO_{2\max SO_2} = 215, \quad (8)$$

$$PO_{2\min MV} = 163 + 25{,}3\dot{V}O_2, \quad (9)$$

$$PO_{2\min CMV} = 175 + 11{,}7\dot{V}O_2, \quad (10)$$

$$PO_{2\min HR} = 202, \quad (11)$$

$$PO_{2\max AVO_2} = 179 + 12{,}3\dot{V}O_2, \quad (12)$$

$$PO_{2\max CUO_2} = 195 + 9{,}5\dot{V}O_2. \quad (13)$$

According to equations 8-13, maximum SO_2 and minimum HR are obtained with constant (unrelated to load level) values of PO_2--215 and 202 mm Hg, respectively. But optimization of other parameters is possible only with elevation of PO_2 as the physical load increases. Maximum changes in PO_2 are required to minimize MV; for this purpose PO_2 of the atmosphere must be raised by 25.3 mm Hg for each liter of oxygen uptake per minute.

As we see, the optimality conditions do not coincide for different parameters of the organism. This shows that a search for the laws of optimum control of environmental parameters can be made only with the use of an integral criterion of the state of body functions. Formulation of such a criterion is a mandatory element in solving the problem under discussion.

Because of the extreme complexity of determination of the required criterion, this question, of course, exceeds the scope of a single paper. With the available information, it is deemed the most expedient to use equation 9 for MV, as an index with maximum sensitivity to PO_2 and rather high degree of integration, as a possible general law in regulating atmospheric PO_2:

$$PO_{2opt} = 163+25.3\dot{V}O_2. \quad (14)$$

Apparently, when using this law of regulation, the required changes in PO_2 are quite sizable within the possible range of loads.

The dynamic control of oxygen content in the SC atmosphere can be implemented in practice by means of systems where not only $\dot{V}O_2$, but other, technically more suitable indices are used as input physiological information: MV, HR, $\dot{V}CO_2$, alveolar PCO_2 and others. Some relevant laws of control can be obtained from the submitted model. In particular, when using the parameter of pulmonary ventilation in the system, as the controlled physiological parameter, the characteristics of optimum PO_2 regulator have the following appearance:

$$PO_{2opt} = 159+0.81MV-0.0015MV^2. \quad (15)$$

It is felt that this approach to control of PO_2 in the respiratory environment can be used in extravehicular and planetary space suits.

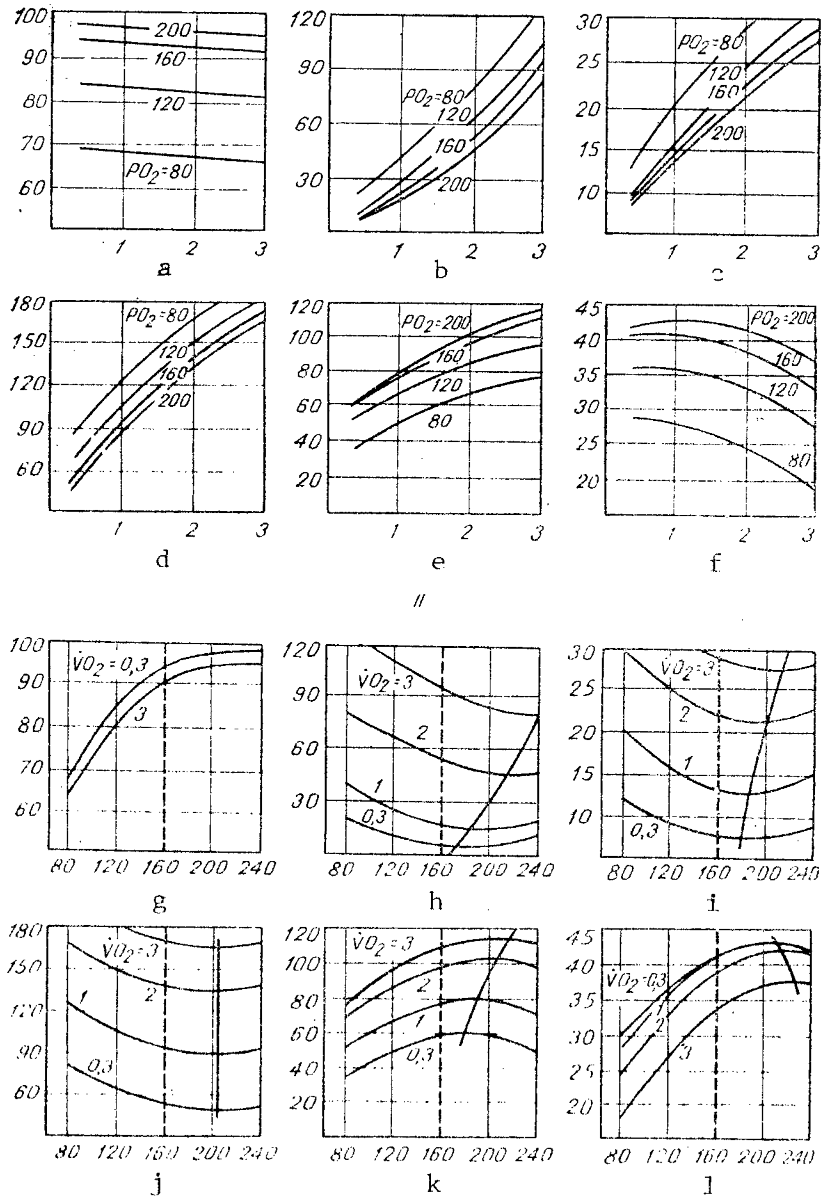

Figure 1. Effect of PO_2 of inspired air and $\dot{V}O_2$ of man in a stabilized state on SO_2, MV, CMV, HR, AVO and CUO_2. The vertical dotted lines refer to value of given physiological parameter with different $\dot{V}O_2$ and normal PO_2; solid line connects extremum points and indicates optimum PO_2 and physiological indices for each VO_2.

I) $\dot{V}O_2$ (liter/min)
II) PO_2 (mm Hg)
a,g) SO_2 (%)
b,h) MV (liters)
c,i) CMV (liters)
d,j) HR (beats/min)
e,k) AVO_2 (ml/liter)
f,l) CUO_2 (ml/liter)

Let us now consider analogously the problem of controlling PCO_2 in the SC atmosphere.

When discussing the problems that arise in regulating the composition of SC atmosphere, one has to take into consideration the possibility of an unforeseen fall of PO_2 due to depressurization of the cabin and other causes that would result in development of hypoxia in the cosmonauts. And, as we know, hypoxic hypoxia is complicated by hypocapnia due to excessive flushing of CO_2 from blood.

One of the possible means of attenuating the adverse effect of a shortage of oxygen is to add carbon dioxide to the inspired air; this enhances the ventilatory reaction to hypoxia and prevents development of hypocapnia. Indeed, in an experiment where PO_2 in the chamber fell by almost 50%, addition to the atmosphere of 2-2.5% CO_2 preserved efficiency of the subjects for up to 2 days [7]. For this reason, some authors have proposed that the SC atmosphere be enriched with carbon dioxide to normalize the functional state of cosmonauts under such emergency situations [5, 6]. However, it has not yet been determined what specific concentrations of CO_2 are required to assure normal exchange of gases in man in the presence of varying levels of oxygen shortage in the atmosphere.

In order to answer this question, one must establish quantitative functions between PO_2, PCO_2 and indices of respiratory function and oxygen supply to the organism. An analysis was made of our experiments, which were pursued to investigate the stabilized reactions of the human body at rest, when breathing gas mixtures with PO_2 ranging from 150 to 70 mm Hg, and PCO_2 from 0 to 40 mm Hg [2]. Thus, a study was made of virtually the entire range of changes in levels of respiratory gases compatible with human vital functions. The mathematical description of the required functions was supplied by the method of multidimensional regression analysis.

Oxygenation of arterial blood is the most informative index of oxygen supply to the organism. Pulmonary ventilation, as well as HR and CMV are functions of this parameter to a significant extent. For this reason, in order to solve the formulated problem, it is first necessary to formulate the influence of factors that determine the SO_2 level. Of course, PO_2 of the respiratory environment is one of these factors. On the other hand, SO_2 can be regulated by controlling pulmonary ventilation.

It was found that, in the presence of a hypercapnic stimulus, static MV is related to PCO_2 of the atmosphere in the following manner:

$$\mathrm{MV} = 8{,}8 + 0{,}12PCO_2 + 0{,}0045PCO_2^2 \quad (\sigma = 2{,}6,\ R = 0{,}79). \qquad (16)$$

The equation shows that MV can increase by almost 100% within the permissible range of changes in PCO_2.

Taking this possibility into consideration, we obtained SO_2 as function of PO_2 and PCO_2 of the respiratory environment:

$$SO_2 = -51,6 + 2,08PO_2 + 0,96PCO_2 - 0,0057PO_2PCO_2 - 0,0073PO_2^2$$
$$(\sigma = 7,1, \quad R = 0,91). \qquad (17)$$

The last equation makes it possible to determine the effectiveness of adding CO_2 to SC atmosphere when PO_2 falls. In particular, one can determine SO_2 for different values of atmosphere PCO_2. It was found, for example, that SO_2 as function of PO_2,, in the absence of CO_2 in the atmosphere and with maximum permissible concentrations thereof (PCO_{2max} = 40 mm Hg in the case of brief exposure), is defined as follows:

$$SO_2 = -51,6 + 2,08PO_2 - 0,0073PO_2^2, \quad PCO_2 = 0 \qquad (18)$$

$$SO_2 = -13,2 + 1,85PO_2 - 0,0073PO_2^2, \quad PCO_2 = 40 \qquad (19)$$

Figure 2 illustrates graphs of these functions. The crosshatched segment of the graph indicates the range of values of SO_2 when ambient PCO_2 changes from 0 to 40 mm Hg.

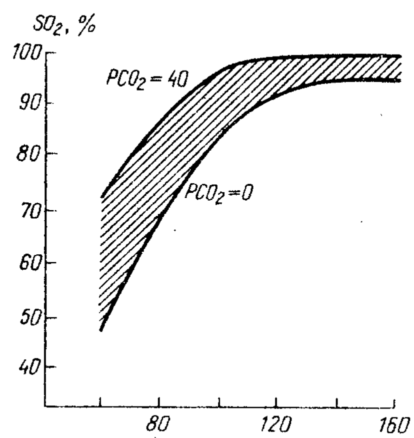

Figure 2.
Range of values of oxygenation of human arterial blood with ambient PO_2 from 160 to 60 mm Hg and PCO_2 from 0 to 40 mm Hg

X-axis, PO_2 (mm Hg)

Equation 17 enables us to determine the static characteristics of a regulator of carbon dioxide level in the SC atmosphere. Such a device could be executed as a system for regulation of perturbance [input effect], where the main input effect to be controlled is lowering PO_2 in the gas environment.

We submit below an equation obtained for such a regulator, the purpose of which is to maintain oxygenation of blood at the 90% level when atmosphere PO_2 falls:

$$PCO_2 = 1,6\ (112 - PO_2), \text{with } PO_2 \leqslant 112 \text{ mm Hg}. \qquad (20)$$

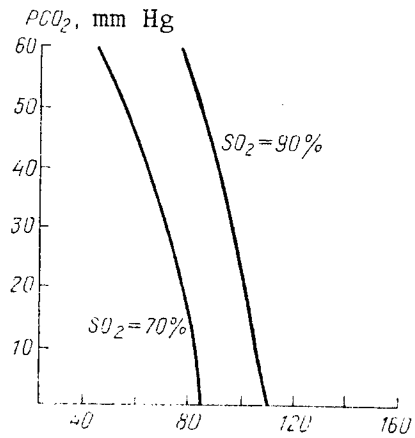

Figure 3.
Partial pressure of carbon dioxide added to atmosphere with lowering of oxygen pressure required to stabilized SO_2 of man, with SO_2 = 90% and SO_2 = 70%.
X-axis, PO_2 (mm Hg)

When it is necessary to hold SO_2 at a level of at least 70%, the characteristics of the PCO_2 regulator appear as follows:

$$PCO_2 = 1{,}8\ (83 - PO_2), \text{with } PO_2 \leq 83 \text{ mm Hg}. \qquad (21)$$

Equations 20 and 21 are a linear approximation of the sought functions, or laws of regulating the body's SO_2 under hypoxic conditions by adding CO_2 to the atmosphere. Figure 3 illustrates graphs of statistical characteristics of the two PCO_2 regulators discussed. By using the patterns obtained for dynamic control of CO_2 content of SC atmosphere, it is possible to optimize oxygen supply for cosmonauts in the case of uncontrollable PO_2 drop.

The questions discussed in this paper had the objective of determining the possibility and patterns of dynamic control of parameters of SC atmosphere as a means of optimizing the functional state of cosmonauts. Unquestionably, the results obtained require further development. It is too soon to determine the purposefulness of the discussed system of biological control of parameters of an SC environment. However, it is obvious that "the longer term prospects related to performance of interplanetary flights advance such research problems as development of closed ecological systems, minimalization of physiological functions and biological control. The solution thereof cannot be postponed..." [8].

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MECHANICS OF SPEECH-RELATED RESPIRATION WHILE PERFORMING STATIC PHYSICAL EXERCISE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 58-63

[Article by M. A. Tikhonov and A. S. Belan, submitted 21 Jul 75]

[Text] Investigation of the distinctions of speech generation in man under different living and functioning conditions is of definite interest to applied physiology, as indicated in particular by the numerous studies of verbal function in aviation, space and diving practice, in the presence of diverse emotional and stress states, etc. [1-5].

However, the biomechanical aspects of speech formation, i.e., the correlation between the latter and mechanical and aerodynamic processes in the lungs and vocal tract, have not been investigated comprehensively enough under such conditions.

Our objective here was to make an experimental study of the mechanics of respiration during speech while performing physical exercises.

Methods

We investigated the distinctions of mechanics of respiration during speech at rest and with a physical load on 12 essentially healthy males ranging in age from 18 to 35 years. For this purpose, the subjects in seated position pronounced a standard phrase without muscular tension and while pulling dynamometer levers toward themselves with a force of 10 kg to a maximum of 80-100 kg.

We recorded volumetric air flow velocity (pneumotachygram) and the integrated curve of respiratory volumes (spirogram) during spontaneous respiration and speech using a mask with built-in Fleisch tube and pneumotachygraph. We measured transpulmonary intrathoracic pressure in the middle third of the esophagus in relation to pressure under the mask in five subjects, using a probe with latex balloon 10 cm long and 1 cm in diameter, filled with 1.5 cm^3 air and a differential electromanometer.

Changes in functional residual volume (FRV) of the lungs during physical exercise were demonstrated using a Krogh spirograph connected to the "bag in a box" system [6].

Synchronous recording of the pneumotachygram, spirogram and transpulmonary intrathoracic pressure enabled us to calculate velocity and volume parameters of pulmonary ventilation, respiratory tract resistance [7], as well to determine subchordal pressure and dynamics thereof during the speech process. In view of the fact that it is quite difficult to measure subchordal pressure directly, we used a method of indirect determination thereof by means of correction of transpulmonary intrathoracic pressure measured in the esophagus [8]. The difference between this pressure and subchordal pressure corresponds to magnitude of static elastic traction of the lungs [9].

We modified this method to fit the conditions of ordinary speech within the range of normal respiratory volumes. For this purpose, we first determined the pressure-volume function for the lungs under quasistatic conditions, i.e., with the slowest possible inspiration in relation to level of maximum inspiration to residual volume and plotted a curve of static transpulmonary pressure as function of change in lung volume (Figure 1, P_{st}). We then recorded intrathoracic pressure in the esophagus during utterance of a standard phrase with varying levels of physical exercise (Figure 2) and plotted these data on the pressure-volume graph. Estimation of volume of phonated* expiration was made as follows: we plotted the volume of prior inspiration on the y-axis, in relation to level of functional residual volume (determined from the level of relaxed expiration in the vital capacity test), and from it we subtracted the expiratory volume during speech, as determined from the integrated spirogram. The sum of intrathoracic pressure during phonation and pressure of static traction of the lungs produces the flow of air from the lungs through the constricted rima. This pressure reflects in essence the level of subchordal pressure (see Figure 1, P_{nc}) that appears during speech as a result of constriction of the rima, since the pressure required to overcome resistance of hypolaryngeal and epiglottic respiratory tracts during spontaneous respiration constitutes only a negligible part of intrathoracic pressure.

Results and Discussion

The Table lists the results of quantitative analysis of volume and rate indices of pulmonary ventilation during ordinary breathing and speech associated with a progressively increasing physical load.

With increase in load, the duration of inspiration prior to phonation diminished, but its volumetric velocity increased, so that the volume of inspiration increased. Inspiration became deeper, faster and intermittent. Transpulmonary pressure acquired a higher and higher negative value, thereby allowing for an increase in velocity of inspiratory flow.

*Hereafter, expiration during speech is referred to as phonated.

Dynamics of parameters of respiratory mechanics during speech with different levels of physical load (M±m)

Indices of respiratory mechanics	Conditions of utterance of phrase				
	without load	physical load (kg)			
		10	20	50	80—100
Duration of inspiration [Ins] preceding speech (s)	1,53±0,02	1,46±0,06	1,42±0,03	1,21±0,02	0,91±0,19
Duration of phonated Ins (s)	6,12±0,06	5,75±0,07	5,91±0,07	5,60±0,05	4,95±0,04
Volume of Ins preceding speech (ml)	726±79	794±37	922±53	970±44	960±41
Volume of expiration [Exp] during speech (ml)	940±93	1038±74	1177±46	1240±51	1250±38
Difference between phonated Exp and prior Ins (ml)	214	244	255	270	290
Maximum volumetric rate of air flow (liter/s):					
in Ins	0,37±0,05	0,43±0,04	0,53±0,05	0,66±0,05	0,98±0,05
in Exp	0,19±0,016	0,22±0,012	0,32±0,03	0,41±0,02	0,45±0,2
Mean volumetric rate of air flow during speech (liter/s)	0,10±0,01	0,13±0,05	0,17±0,02	0,18±0,01	0,22±0,03
Maximum intrathoracic pressure during Ins (cm water)	—4,3±0,25	—8,0±0,34	—7,7±0,56	8,7±0,48	—9,4±0,84
Maximum subchordal pressure during speech (cm water)	15,0±1,1	20,6±1,3	21,0±1,3	28,6±1,8	32,2±2,4
Mean resistance to expiratory flow during speech (cm water/liter/s)	44,0±1,6	56,0±2,1	62,0±2,7	50,0±2,3	56,0±3,9
Respirator tract resist. (cm w./ l/s): during Ins	2,4±0,17	2,8±0,27	2,7±0,24	3,3±0,39	3,9±0,26
during unphonated Exp	2,9±0,14	2,8±27	2,7±0,24	3,3±0,39	3,9±0,26

There was also a decrease in duration of expiration during utterance of the phrase, but it was less marked than that of the prior inspiration, mainly due to the fact that with large and maximum loads there were pauses in flow of air prior to the start of expiration, against a background of maximum elevation of intrathoracic pressure (see Figure 2). There was negligible change in duration of phonation proper.

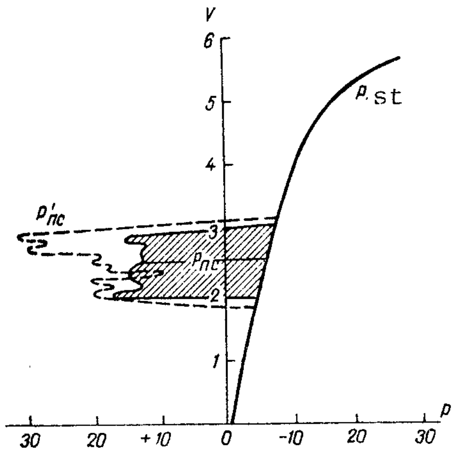

Figure 1.
Subject L-v. Pressure-volume function for the lungs and dynamics of hypolaryngeal pressure during speech.
Y-axis, vital capacity of lungs (liters); x-axis, transpulmonary intrathoracic pressure (cm water).
P_{st}) static transpulmonary pressure
P_{nc}) subchordal pressure during speech at rest
P'_{nc}) subchordal pressure during speech under 50-kg physical load

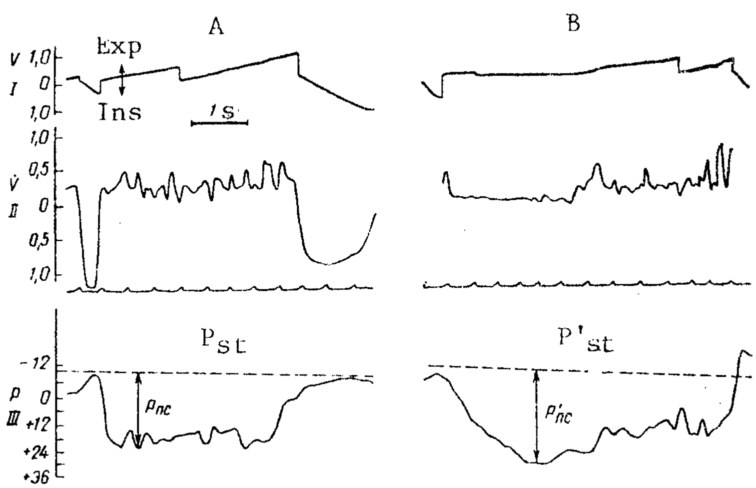

Figure 2. Subject L-v. Effect of physical load on expiratory dynamics during speech.

A) speech at rest
B) with 50-kg physical load
I) integrated spirogram (liters)
II) pneumotachygram (liter/s)
III) intrathoracic transpulmonary pressure (cm water)
Ins) inspiration
Exp) expiration

The volume of phonated expiration was consistently greater than the volume of prior inspiration, and this difference increased with increase in load. Furthermore, we observed a decrease in lung volume (with a 50-kg load, FRV decreased by 480±56 cm^3).

With increase in load, subchordal pressure rose significantly, and with a maximum load it increased by over 100%.

There was about the same change in maximum values of expiratory flow rate, and the rate peaks were often shifted toward the end of the phrase (see Figures 2 and 3), which could apparently be attributed to dilation of the rima.

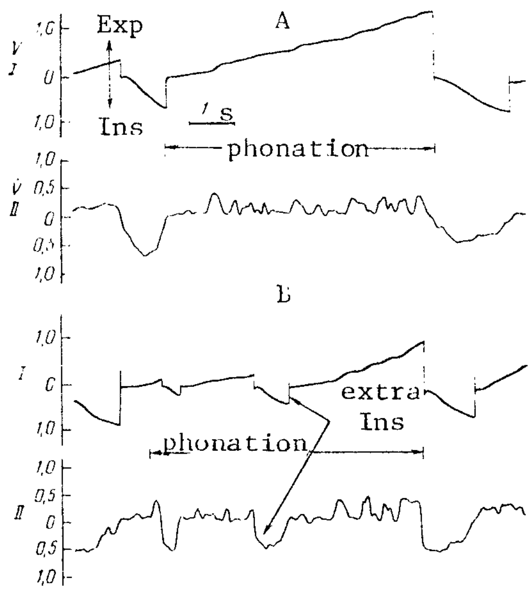

Figure 3.
Subject Sh-y. Changes in volume and rate indices of pulminary ventilation during speech
A) at rest
B) maximum load
I) integrated spirogram (liters)
II) pnemotachygram (liter/s)

Figures 1 and 2 show that subchordal pressure of subject L-v fluctuated in the range of 18-24 cm water during phonation at rest and increased to 26-38 cm water with a 50-kg physical load.

Figure 3 shows that the configuration of pneumotachygrams of a standard phrase with a physical load can be reproduced rather readily; however, with large loads, 50 kg or more, phonated expiration is often interrupted by one or two extra inspirations.

There was no appreciable change in resistance of respiratory tract during inspiration with a load; during an ordinary expiration, without phonation, it increased somewhat (apparently due to diminished cross section of respiratory tract with reduction of lung volume). There was a sharp increase (about 20-fold) in respiratory tract resistance during speech, as compared to nonphonated expiration, due to narrowing of the rima.

It is known that the lungs have a second function consisting of creating pressure in the subchordal space to assure a flow of air through the rima and vibration of vocal cords, in addition to their main function, i.e., exchange of gases. We know that there is a co-relation between level of subchordal pressure, velocity of air flow and volume of sound during continuous phonation (singing) in expiration in the volume of vital lung capacity (VC)[10, 11].

As a result of this investigation, several changes were demonstrated in time, velocity and volume parameters of pulmonary ventilation during speech, interpretation of which is based on analysis of dynamics of subchordal pressure and air flow through the rima.

In particular, the appearance of extra inspirations during speech with a physical load is apparently attributable to the fact that, with increase in static physical tension, there is a decrease in lung volume due to contraction of thoracic and abdominal muscles. In addition, expiration is associated with increasing mean, as well as maximum velocities of air flow against the background of reduced lung volume, as a result of which the volume of air in the lungs is insufficient to implement the complete volume of phonated expiration, which leads to extra inspirations that interrupt the flow of speech.

Proprioceptive impulsation from receptors of muscles and ligaments of the thorax, which is directed toward attaining the lung volume at which speech usually begins and retention of the customary stereotype of phonated expiration, apparently has some significance as well.

The resistance of the respiratory tract is the integral index of aerodynamic processes in the lungs and vocal tract during speech. Like other authors [10], we observed a sharp increase therein during phonation, as a result of constriction of the rima. This resistance was about 20 times greater than total resistance of intrathoracic and extrathoracic respiratory tracts during ordinary respiration.

Resistance of the larynx fluctuates over a wide range: 5-10 cm water/liter/s when uttering consonants and up to 70-100 cm water/liter/s when uttering vowels.

We observed fluctuations of resistance from 18 to 72 cm water/liter/s during ordinary speech associated with rapid alternation of vowel and consonant sounds, against the background of a relatively stable mean level of order of 44-62 cm water/liter/s at rest and with different physical load levels. Consequently, it can be concluded that high intrathoracic pressure, which aids in immobilization of thoracic and abdominal muscles during static tension of postural muscles, does not have an appreciable effect on laryngeal resistance, due to approximately equal increase in intrathoracic pressure and velocity of air flow.

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ELECTROLYTE CONTENT OF BLOOD AND POTASSIUM ION TRANSPORT IN ERYTHROCYTES OF ANIMALS EXPOSED TO A STEADY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 63-67

[Article by G. K. Gerasimova and Z. N. Nakhil'nitskaya, submitted 1 Oct 75]

[Text] Technological progress is posing an increasingly acute question of influence of a high-tension steady magnetic field (SMF) on the human body. This problem is also a pressing one for physical laboratories and many branches of industry. In recent years, there has been discussion in the literature of the possibility of using high-power magnetic fields to protect the crew of spacecraft from ionizing radiations in the course of prolonged flights [1, 2]. The existing experimental data are indicative of the biological activity of magnetic fields; however, few clearcut results have been obtained. Several questions were overlooked by researchers. For this reason, it is not yet possible to derive unequivocal conclusions as to the nature and extent of SMF effects on the human body. In particular, not enough work has been done on the question of SMF influence on electrolyte metabolism in the entire organism and in the cell. Maintenance of constant concentrations of alkaline metal ions is important to normal vital functions of both the whole organism and its different systems and cells. At the same time, we know that there is a decline of levels of potassium, sodium and chloride ions in blood, with concurrent tendency toward increase in calcium ions in human blood following 15-60-min local exposure to SMF of 1000 Oe [3]. It has been reported that there is a reliable increase in excretion of potassium and sodium ions in urine of mice exposed to 14 kOe SMF for 24 h and 7.2 kOe for 96 h [4], as well as changes in potassium, sodium and calcium ion levels in blood and other mouse organs after exposure to 5000 Oe SMF [5] for 1-6 days, and in the blood of rabbits after exposure of the head to SMF of 2000 and 4000 Oe [6]. It is assumed that strong magnetic fields affect migration of sodium ions through biological membranes [7, 8].

Our objective was to determine the nature and extent of SMF influence on concentration of potassium and sodium ions in blood, distribution thereof in plasma and erythrocytes, blood pH and erythrocyte volume in animal blood, as well as transfer of potassium ions through the erythrocyte membrane in in vitro experiments.

Methods

Male rats weighing 180-220 g, in a plexiglas box, were placed in the field of an SP-15A electric magnet with flat parallel pole shoes 400×300 mm in size. They were 100 mm apart. The magnetic field was virtually uniform in the central part of the interpolar space 300×200 mm in size, and voltage drop in the rest of the space did not exceed 15-20% of the level in the middle. Voltage pulsation constituted 1.8%. The south pole was referable to the top polar shoe. Field voltage was measured with a type Ye-11-3 magnetic induction gage. The error factor of the instrument constituted $\pm(1.5+100/H)\%$, where H is force of the field (in Oe). Control animals were kept in the same room as the experimental ones. The magnetic field in the area of the control animals did not exceed 1.5 Oe. We conducted six series of experiments differing in duration of exposure of animals to the magnetic field (1, 3, 24 h and 15 days) and force thereof (1000 and 4500 Oe). In one of the series, the animals were exposed repeatedly to 4500 Oe SMF for 3 h daily, for 5 days. Blood was taken by decapitating the animals. We assayed potassium and sodium ion content of blood and plasma by flame photometry, erythrocyte volume according to the hematocrit index, and blood pH on a micro-pH-meter. The tests were made at the early post-exposure stages: 1 and 3 h after discontinuing exposure, and in the series with 3-h exposure to 4500 Oe SMF after 5 days as well. We evaluated transport of potassium ions through the erythrocyte membrane according to the values of coefficients K_{ab} and K_{ba}, which characterize transport of potassium ions from plasma to the cell and from the cell to plasma. For this purpose, we used radioactive potassium (^{42}KCl and $^{42}K_2CO_3$). Tests were made on eluted erythrocytes of white rats suspended in a mixture of buffer solution and plasma (10:1 ratio). The erythrocyte suspension was put in a water bath at 37° in a 4500 Oe magnetic field for 3 h. We determined the transport coefficients during the 1st and 3d h of incubation in the SMF. For this purpose, at the beginning of the 1st and 3d h of incubation, we added the isotope to the test tubes with erythrocyte suspension at the rate of 7 µCi per ml suspension, and then took samples every 20 min to estimate regression of radioactivity of plasma, hematocrit index, potassium content in the erythrocyte suspension and in the incubation medium. Radioactivity was counted on a PST-100 unit. We calculated the coefficient of potassium ion transport from plasma to the cell, K_{ab}, using the following formula:

$$\frac{\Delta C_p}{C_p} = K_{ab}\Delta t,$$

where C_p is the initial concentration of plasma ^{42}K, and ΔC_p is change thereof in time Δt. The slope of the absorption curve was calculated by the least squares method. The coefficient of potassium ion transport from the cell into plasma was calculated using the following formula:

$$K_{ba} = K_{ab} \cdot \frac{C_p}{C_q} + \frac{1-H}{H} \cdot \frac{1}{C_q} \cdot \frac{\Delta C_p}{\Delta t}$$

where K_{ab} is the transport coefficient in the plasma--cell direction; C_p is mean potassium concentration of plasma during incubation period; C_q is mean concentration of potassium in the cell during incubation period; ΔC_p is change therein in time Δt; H is hematocrit index.

Results and Discussion

Exposure to SMF induced changes in potassium and sodium ion content of the animals' blood and plasma. We could detect lowering of concentration of $K^{\cdot}$ and elevation of $Na^{\cdot}$ in the blood and $K^{\cdot}$ in plasma 1 hour after exposure to 3400 Oe SMF for 1 h. At this time, the $K^{\cdot}$ and $Na^{\cdot}$ levels in blood of experimental animals constituted 147.0±4.4 and 209±12 mg%, versus 162.5±2.4 and 178.2±2.2 mg%, respectively, in the control. $K^{\cdot}$ content of blood plasma in the experimental group of animals rose to 23±2.8 mg%,1 h after exposure, versus 16.3±1.7 mg% in the control. Some of the observed changes were transient. The electrolyte levels in blood reverted to initial values 3 h after exposure, whereas blood plasma $K^{\cdot}$ concentration still remained high. After 3-h exposure to 4500 Oe SMF, the blood of experimental animals showed a decline of Na concentration. This was observed 1 h after exposure and it persisted for the next 5 days. At this time, there were maximum changes in $Na^{\cdot}$ content. $Na^{\cdot}$ concentration constituted 156.3±2.2 mg% on the 5th day after exposure, versus 178.2±2.2 mg% in the control; it constituted 166±2.5 and 170±0.2 mg% 1 and 3 h after exposure, respectively. We failed to demonstrate changes in blood $K^{\cdot}$ content and blood plasma $K^{\cdot}$ and $Na^{\cdot}$ after 3-h exposure. The changes in blood electrolyte content were less consistent after exposure to 1000 Oe SMF.

After 1-h exposure, we observed a transient decline of blood $Na^{\cdot}$ content 1 h after exposure. Its concentration constituted 169±2 mg% in experimental animals, versus 185.5±6.7 mg% in the control. The concentration of potassium ions in blood and plasma did not exceed the range of control levels 3 h after exposure. We failed to demonstrate deviations referable to the other indices studied with such exposure. There were no cumulative effects when exposure time was increased. On the contrary, after both 1- and 15-day exposure, during the period of immediate after-effects, no change was demonstrated in blood $Na^{\cdot}$ content, although such a change was typical after 1-h exposure, and this is indicative of the possibility of recovery of $Na^{\cdot}$ content during exposure. With increase in exposure time there was a tendency toward higher $K^{\cdot}$ content in plasma. Its level was 1.6 mg% above the control after 1-day exposure. No changes were observed in blood and blood plasma $K^{\cdot}$ content with 15-day exposure. Cumulative effects were also lacking in the case of repeated exposure. A study of changes in blood electrolyte content following daily 3-h exposure to SMF of 4500 Oe for 5 days revealed that the decline in blood $Na^{\cdot}$ concentration observed immediately after the first exposure does not progress thereafter with increase in number of exposures. The differences between experimental and control animals leveled off, with regard to $Na^{\cdot}$ content of blood, after three and five exposures. At the same time, differences in concentration of $K^{\cdot}$ of blood appeared only after the fifth exposure. They coincided in direction and magnitude with the changes demonstrated 5 days after single 3-h exposure to a field of the same force. We failed to demonstrate changes in plasma $K^{\cdot}$ and $Na^{\cdot}$ content after five exposures. The concentrations of $K^{\cdot}$ and $Na^{\cdot}$ constituted 18±1.2 and 325±7.3 mg%, respectively, in the control and 16±1.5 and 314±6.6 mg% in the experimental group. The pH and erythrocyte volume in blood of experimental animals did not undergo any changes. Only in the series of tests with 1-h exposure to

SMF of 4500 Pe did we observe a statistically reliable decrease in blood erythrocyte volume 1 hour after exposure. It was transient and the level reverted to normal in the 3d postexposure hour.

Experiments with incubation of erythrocytes in a SMF revealed that there is no increase in gradient yield of potassium ions in the incubation medium during exposure. Thus, after 1-h incubation in a 4500-Oe SMF, $K^{\cdot}$ concentration in the incubation medium constituted 15.1±1.70 mg%, versus 14.8±0.38 mg% in the control; after 3-h incubation the figures were 15.9±0.74 mg%, versus 15.1±0.05 mg% in the control. The results of estimation potassium ion transport through the membrane of erythrocytes incubated for 1 h and 3 h in a 4500-Oe SMF at 37°C indicate that the SMF does not affect transport of potassium ions into the cell and from the cell into plasma. The Table lists the coefficients characterizing transport of potassium ions through the erythrocyte membrane. We see that with both 1- and 3-h exposure the coefficients of potassium ion transport from plasma to cell and from cell to plasma, as well as the overall flow of potassium ions in both directions, do not differ from control values.

Potassium ion transport through erythrocyte membrane after exposure to 4500-Oe SMF varying in duration

Exposure time (h)	K_{ab}	K_{ba}	$K^{\cdot}$ concentration in plasma (mg-equiv/1 cells/h)	$K^{\cdot}$ flow into cell (mg-equiv/1 cells/h)	$K^{\cdot}$ flow from cell to plasma (mg-equiv/1 cells/h)
Experiment n = 9	0,736±0,046	0,034±0,002	4,34±0,410	3,44±0,230	3,05±0,175
1 Control n = 9	0,763±0,053	0,033±0,004	4,16±0,316	3,45±0,198	3,06±0,164
Experiment n = 6	0,765±0,069	0,035±0,005	4,07±0,231	3,27±0,450	3,11±0,393
3 Control n = 6	0,774±0,035	0,033±0,002	3,85±0,013	3,20±0,114	2,94±0,114

Thus, the results of these experiments indicate that 1- and 24-h exposure of animals to 1000-Oe SMF does not elicit appreciable changes in concentration of potassium and sodium ions in blood. An increase in force of SMF to 4500 Oe is associated with some variability of changes in electrolyte composition of blood. The reliable increase in plasma $K^{\cdot}$ concentration and transient decrease in level thereof in blood should be considered the most distinct changes in the case of 1-h exposure. With 3-h exposure, the most distinct change is the decreased concentration of $Na^{\cdot}$ in blood. Repeated and prolonged continuous exposure does not lead to summation of effects. The demonstrated changes are not pathological in nature, and they do not exceed the range of physiological fluctuations. The lack of changes, in our experiments, in coefficients of potassium ion transport through the erythrocyte membrane does not rule out the possibility that SMF affects transmembrane

transfer of ions during exposure. To answer this question, special methodological approaches are needed that would not require long treatment of the substrate after discontinuing exposure, when rapid recovery from changes observed in the field is possible.

The pH and volume of blood erythrocytes did not undergo any changes.

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HEMOPOIESIS IN DOGS EXPOSED TO LETHAL DOSES OF PROTONS WITH SHIELDED BONE MARROW

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 67-70

[Article by G. F. Nevskaya, G. M. Abramova, Ye. V. Ginsburg, D. N. Ishmukhametova, and A. S. Skorik, submitted 2 Dec 74]

[Text] At the present time it is unquestionable that shielding of part of the bone marrow during exposure to acute radiation attenuates sharply the biological effect of radiation. This is a pressing problem in order to assure radiation safety of space missions.

In order to solve problems of space radiobiology, it is interesting to investigate the long-term effects of nonuniform irradiation by protons which, as we know, are the main component of solar burst radiations.

Results and Discussion

Our studies are referable to the results of 6-year observation of 18 dogs exposed twice to minimum absolutely lethal doses (350 rad) of protons at a 45-day interval. Shielding of 10% of the bone marrow in the region of the head (5 animals), 13% in the region of the chest (5), 5% in the abdominal region (4) and 14% in the pelvic region (4 animals) resulted in survival of the dogs.

In the acute period of radiation sickness the changes in all formed elements of peripheral blood, with the exception of erythrocytes, were considerably more severe in dogs exposed to radiation with the abdomen shielded. Thereafter, at longer intervals following irradiation, these differences gradually levels off, although hemopoiesis remained deficient for several years in animals irradiated with protection of the abdominal region. There were still very marked differences in amount of elements studied 1.5 months after exposure, in animals with shielded abdomen and in dogs in the other experimental groups. However, starting in the 3d month of observation, the differences became statistically unreliable. On the whole, over the entire observation period, in all groups of dogs the leukocyte count did not reach base levels, ranging from 60 to 85% for the first 3 years and holding at the 70-90% level thereafter.

Interestingly enough, according to the data of N. K. Yevseyeva [3], in healthy dogs of the same age maintained under the same conditions as our animals, the leukocyte count began to drop gradually when they reached 3 years of age, and by the age of 4-5 years it constituted 65-75% of the initial level. On the basis of these data, it can be stated that as early as 2 years after irradiation the leukocyte level in irradiated dogs in our experiments was within the physiological range. Nevertheless, the total number of these cells in peripheral blood does not determine leukopoiesis in the organism, and there are quite a few signs that suggest it did not revert to the initial level in irradiated animals.

First of all, we found that absolute lymphopenia and neutropenia persisted, even 5-6 years after irradiation of the dogs, and animals exposed to radiation with the abdomen shielded presented no more than 75% lymphocytes in blood at any of the examination times. Along with quantitative changes, there were deviations in morphological structure of leukocytes. We found segmented lymphocytes and monocytes, hypersegmented neutrophils, binuclear cells or cells with vacuolized nucleus and protoplasm, as well as other degenerative forms of leukocytes. The thrombocyte content of blood did not revert to the initial level either, although some of the tests revealed that the number of such cells in animals of some groups was close to the background values. The dogs gradually developed anemia in the course of the observation period (see Table).

Red blood cells indices in dogs 4.5 years after two exposures to proton radiation in a dosage of 350 rad with local shielding of the body (M±m)

Red blood cell index	Numerical value of indices: before radiation	Numerical value of indices: after radiation	p
Erythrocytes:			
absolute	7,1±0,22	6,2±0,2	< 0,02
%	100	87±4,7	
Hemoglobin	13,8±0,11	12,9±0,46	< 0,05
Color index	0,58±0,017	0,62±0,027	> 0,05

Changes in medullary hemopoiesis occurred concurrently with those in peripheral blood.* While the composition of bone marrow in dogs exposed to radiation with shielded head, chest and pelvis did not show an essential difference from the initial composition after termination of the acute period of radiation sickness, in animals exposed to radiation with shielding of the abdomen there was impairment of proportions between cellular elements on the myelogram (Figure 1). There was severe irritation of the reticular storma of bone marrow, as indicated by the significant increase in number of reticular cells,

*M. P. Kalandarova conducted the observations for the first 3 years.

plasmacytes and monocytes (16.8%). There was also an elevated lymphocyte level. There was also a significant increase in erythroid stem cells (to 19.2). Thereafter, for over 3 years of observation, these differences in medullary hemopoiesis persisted in animals exposed to radiation with the abdomen shielded and in animals of other experimental groups. However, the situation changed 5.5 years after irradiation. While functional activity remained at the same level at this time in bone marrow of animals exposed to radiation with the abdomen shielded, there was a perceptible change in dogs with shielded thorax, head and pelvis. As a result, the bone marrow findings were identical in animals of all groups. As can be seen in Figure 1, which illustrates comparative hemopoiesis in dogs irradiated with shielding of the chest and abdominal region, the quantitative proportions of cellular elements on the myelograms were markedly altered. There was a sharp decrease in red stem cell level with relatively unchanged white stem cell level and the leuko-erythroblast index was greater than 2. We observed irritation of reticular stroma and an increase in levels of lymphoid elements. There were fewer than 2% young forms of granulocytes. Analogous changes were demonstrated in dogs exposed to radiation with the head and pelvis shielded.

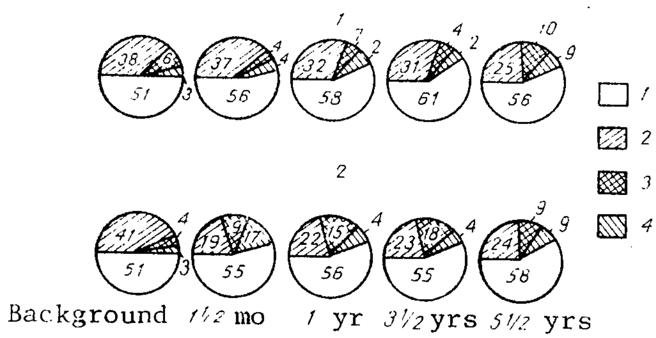

Figure 1. Bone marrow of dogs at different times following two-fold exposure to protons in a dosage of 350 rad, with shielding of the chest (1) and abdomen (2)

Comparative dynamics of changes in bone marrow indices of the dogs, as compared to the initial data, are illustrated in Figure 2, which shows that in the presence of significant depression of functional activity of erythroblasts there is marked proliferation of reticular stromal cells. As we know, intensified proliferation of reticular cells, with limited capability for differentiation thereof, can create the conditions for development of leukemia [1, 2, 4-7, 9].

It is assumed that, in the case of exposure to nonuniform radiation, there is no excessive proliferation of reticular cells because of preservation of some of the hemopoietic elements. Attenuation of the leukemogenic effect in the case of irradiation with shielding of bone marrow is usually

considered in relation to the foregoing. It is believed that when bone marrow foci are protected restoration of hemopoiesis occurs primarily due to preservation of stem cells under the shield, whereas in the case of total-body irradiation regeneration of blood occurs at the expense of surviving but damaged cells. However, it should be borne in mind that shielded bone marrow functions like a compensatory site only in the acute period of radiation sickness. At the later stages, there is inevitable resumption of activity of hemopoietic tissue in the irradiated parts of the body. Since, according to current conceptions, disturbances referable to the chromosomal system of formed blood elements are the pathogenesis in development of leukemia, there are no grounds to expect elimination of the leukemogenic effect in the case of nonuniform irradiation.

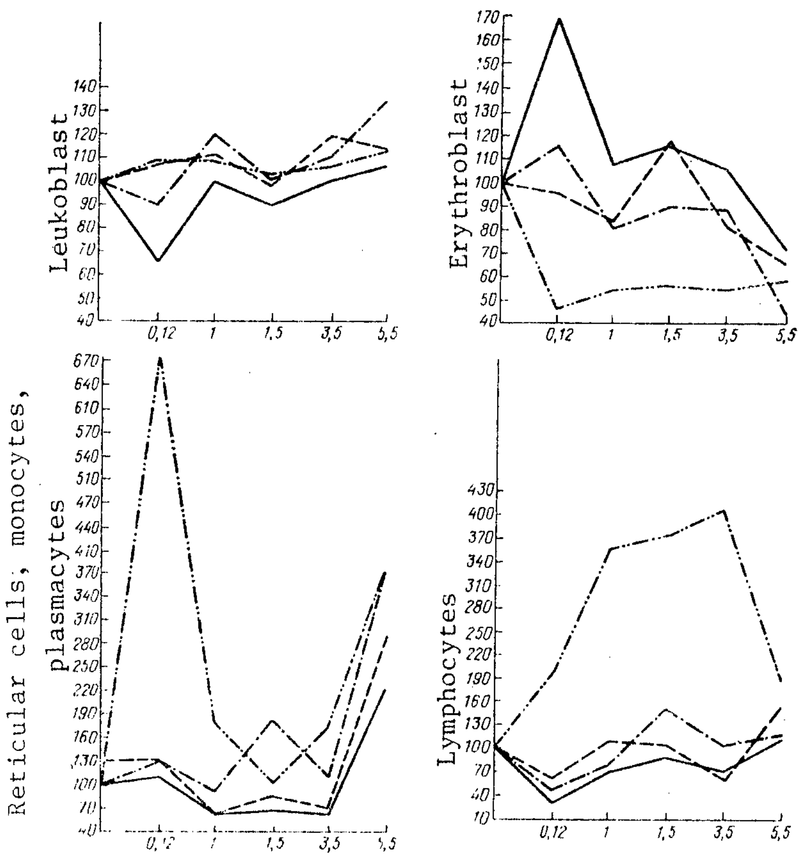

Figure 2. Formed bone marrow elements in dogs following two-fold exposure to proton radiation in a dosage of 350 rad with shielding of the head (solid line), chest (dash line), abdomen (dotted line) and pelvis (dash-dot line)

As we know [9], in spite of the predominantly nonuniform type of irradiation of Japanese victims of atomic explosions, there was a higher incidence of leukemia. In our experiments, no development of leukemia was observed in

dogs over the 6-year follow-up period, in spite of the fact that they were exposed to doses known to be leukomogenic. Probably this is attributable to the natural insusceptibility of these animals to this disease. Nevertheless, hypoplastic hemopoiesis with marked proliferation of the reticular stroma, which they did develop, could be equated, in our opinion, with a preleukemia state in man. It should be noted that such a hemopoietic reaction was encountered for 7-9 years in Hiroshima and Nagasaki among individuals exposed to radiation in doses of 100-500 rad [10].

The obtained data indicate that the bone marrow should apparently be considered a critical organ, not only in the acute period of radiation sickness, but at the long postradiation term after exposure to a range of doses that elicits primarily damage to hemopoietic organs.

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UDC: 574.682:576.8:635.116

INVESTIGATION OF CONCOMITANT MICROFLORA IN PROLONGED SUBSTRATE-FREE CULTIVATION OF BEET PLANTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 71-74

[Article by L. S. Yunusova and N. A. Drugova, submitted 26 Jul 74]

[Text] Studies are being pursued of the material balance of plants, when cultivated by the substrate-free method, as well as the possibility of using the same nutrient solution, with no changes, for long-term cultivation of plants, for the purpose of including higher autotrophs in closed ecological systems. However, in experimental ecological systems, such cultivation cannot be based solely on providing balanced nutrient media without taking into consideration vital functions of microflora. For this reason, the question of correlations between higher plants and microorganisms is an important one to ecology of bioregenerative systems.

In biological systems of life support with higher plants, their bacterial composition will influence formation of the environment of sealed objects as well. Consequently, we must study more than the role of microorganisms in development of plants.

In spite of the fact that there are a number of current works dealing with amounts of microorganism surrounding the root systems of plants, there is still no clearcut conception as to whether it is beneficial for the plants to have a large amount of microorganisms on the root surface and whether there is a certain population level that provides for an optimum correlation between the plants and microflora [2].

Our objective was to investigate the dynamics of microorganism population size in the case of long-term substrate-free cultivation of beet plants, as well as their qualitative and quantitative composition.

Methods

Bordeau variety of beets were cultivated by the hydroponic method in two permanent nutrient solutions differing in salt concentration: 1) Chesnokov

solution; 2) balanced solution of macroelements in 10-100 times lower concentration ("aqueous background"). In the course of the experiment, the solutions were constantly adjusted with regard to elements of mineral nutrition in accordance with consumption thereof by the plants. The initial material for the cultures were samples of nutrient solutions in which plants had been cultivated, as well as washings from the roots. We took samples every 2 weeks and inoculated them on nutrient media. In order to determine the amount of bacteria we used the Koch cup method. We used meat-peptone agar (MPA) and cabbage medium No 19, which is recommended as the optimum medium for epiphytic microflora [3], as the nutrient media.

Elective media were used to study specific groups of microorganisms. Actinomycetes were studied on starch-ammonia agar and fungi on acidulated wort agar (WA), with a pH of 6.0. We used the method of azotobacter growth around rootlets in concentrated Ashby medium for demonstration of aerobic nitrogen-fixing microorganisms. We also studied oligonitrophil forms on unconcentrated Ashby medium, and sporulated ones on MPWA (MPA and WA in a ratio of 1:1).

The method of maximum dilutions in liquid nutrient media was used for group analysis of the following physiological groups of microorganisms: 1) ammonification bacteria on meat-peptone broth; 2) denitrifying bacteria on Gil'taya medium; 3) anaerobic nitrogen-fixing bacteria on organic nitrogen-free medium of Vinogradskiy; 4) cellulose anaerobes on Omelyanskiy medium with filter paper; 5) cellulose aerobes on medium proposed by Yu. M. Voznyakovskaya; 6) nitrifying bacteria on inorganic Vinogradskiy medium.

We then counted the number of microorganisms using the McCready table. Conventional techniques were used to isolate microorganisms in pure cultures and to assay them [4].

Results and Discussion

It is apparent from the results obtained that the bacterial number, determined from growth of microorganisms on MPA increases in both nutrient solutions toward the period of intensive increment of beetroots, i.e., by the 91st day, and then it diminishes by harvesting time (Figure 1); there are more microorganisms in Chesnokov solution than in the "aqueous" variant. As was to be expected, there were many more root-related microorganisms, as compared to total bacteria in both nutrient solutions, but the nature of their development was the same in all variants.

Figure 1.
Dynamics of microorganism population size during long-term substrate-free cultivation of beets. Here and in Figures 2-4: x-axis, time (days); y-axis, number of microorganisms (millions per ml solution and g roots). Solid line, root microflora; dash line, microflora in Chesnokov solution; dash-dot line, microflora in "aqueous" variant

Identification of microorganisms according to physiological groups revealed that there were nitrogen-fixing, ammonifying and denitrifying organisms, as well as oligonitrophils, aerobic cellulose-decomposing organisms and a small amount of fungi. We failed to demonstrate nitrifying and sporogenic microorganisms.

As can be seen in Figure 2, there is a decrease in number of oligonitrophils in solutions on the 49th day and, at about the same time, there is appearance of a representative of bacteria that fix atmospheric nitrogen, the azotobacterm which is apparently related to temporary decrease in nitrogen content of the nutrient medium. However, after the increase in oligonitrophils on the roots by the 49th day their number remains the same thereafter. Unlike oligonitrophils, ammonifyers and denitrifyers in nutrient solutions present a sharp increase by the end of the vegetation period (Figures 3 and 4). But on the roots the amount of denitrifying bacteria diminishes in the course of development of the plants, while that of ammonifying bacteria increases. A study of denitrifying microorganisms revealed that only some of them are genuine denitrifyers. Cellulose-decomposing aerobic microorganisms began to appear in the middle of the vegetation period, and this was probably related to the start of necrosis of root hairs, and toward the end of the vegetation period a negligible amount of fungi also appeared.

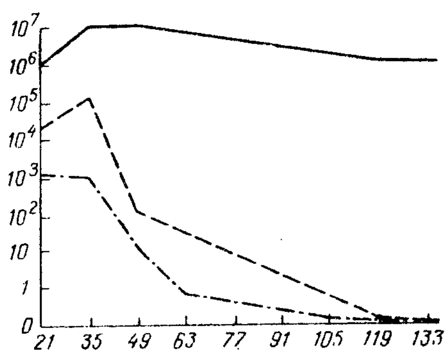


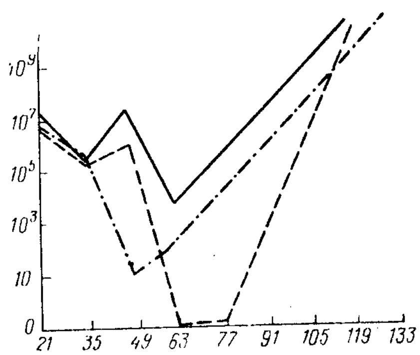
Figure 2.
Change in amount of oligonitrophils during vegetation of beets (millions per ml solution and gram roots)

It should be indicated that we failed to observe any particular differences in development of garden beets on the nutrient solutions mentioned, but there was a difference in amount of nutrients in the leaves and roots.

There was more sugar in the leaves of plants cultivated on an "aqueous background" than in beets grown on a mineral background, but less starch. The same pattern is more pronounced in the roots. Cellulose content of the leaves and roots does not differ in the variants. In young plant roots cultivated in Chesnokov solution there was 2-3 times more ascorbic acid.

The differences in nutrient content result in specific accumulation thereof. In plants cultivated in Chesnokov solution, carbohydrates are present mainly in the form of starch, and in those raised in a water background, in the

form of monosaccharides and disaccharides. Accumulation of ascorbic acid follows the same patterns as were noted in levels thereof.



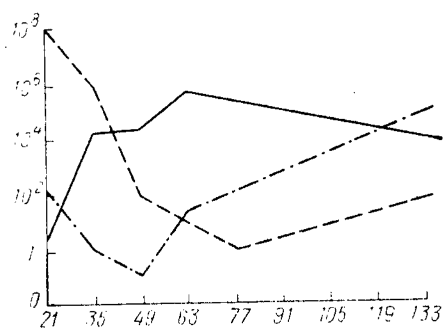


Figure 3.
Development of ammonifying bacteria during growth of beet plants

Figure 4.
Development of denitrifying bacteria during growth of beet plants

(billions per ml solution and gram roots)

Perhaps the above difference in quality of harvest in the experimental variants also affects the nature of accumulation of concomitant microflora. Confirmation of this aspect requires further parallel study of the quantitative and qualitative composition, dynamics of microflora concomitant in higher plants, and direction of biosynthesis of nutrients.

We made an identification of the dominant forms of microorganisms isolated in the course of prolonged cultivation of beets. We found that the majority of bacteria were referable to Pseudomonas and Mycobacterium. Representatives of the genera Bacterium, Micrococcus, Mycococcus, Chromobacterium and Pseudobacterium are also encountered.

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METHODS

UDC: 612.014.47-064].001.57

PHYSIOLOGY OF ANTIORTHOSTATISM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 75-76

[Article by K. L. Geykhman and M. R. Mogendovich, submitted 29 Jul 75]

[Text] It is extremely difficult to find experimental solutions to physiological problems of weightlessness, since it is impossible to fully simulate weightlessness on earth. Nevertheless, some advances have been made in this area [4].

Among the methods of modeling weightlessness, which are used to investigate the dynamics of physiological systems and, first of all, the cardiovascular system, particular importance is now being attributed to the antiorthostatic [head down] position. The "head down" position had occasionally been used in pathophysiological experiments on animals as a unique functional test for evaluation of circulation in man [28]. A semblance of this position is used in surgery (Trendelenburg position). Until recently, the "head down" position had been only considered as a methodological procedure of little importance. This question remained little studied in space physiology as well. Yet the field of antiorthostatism is of basic importance to the solution of a number of problems of normal and pathological physiology [29]. Tests using a tilted table have recently been adopted in experimental physiology at English universities [44].

We began to use this position in 1962 to simulate accelerations and weightlessness in man, and we introduced the corresponding concept of "antiorthostatism." And we make a distinction between passive and active antiorthostatic positions. Their mechanisms are somewhat different: the passive position is related to muscular relaxation, whereas the active one involves voluntary muscular tension, particularly with reference to the hands, for example in hand stands.

Physiology of antiorthostatics was investigated extensively and on a theoretical basis in the Perm' Laboratory for the last 12 years [6, 7, 9-16, 24, 36-41]. In the compendiums that have been published since 1968, "Biomedical Studies in Weightlessness" [32] and "Physiology in Space Environment" [43], nothing was stated about physiological research on antiorthostatics, and

even this term did not yet exist. Subsequently, R. M. Bayevskiy [5] studied antiorthostatism, and he considered it a valuable prognostic test. Yugoslav authors [42] used the "head down" vertical position for 60 s and recorded indices of the EKG, velocity of pulse wave and rheoencephalography. Changes in the sensory system are studied in weightlessness [3, 27]. The changes in various parameters of circulation, which occur in weightlessness in astronauts [25, 26], are consistent with these experimental data. Thus, in weightlessness there is redistribution of blood and increased filling of venae cavae, right atrium, vessels in the pulmonary circulation and left atrium. Ye. A. Kovalenko [26] writes: "... cosmonauts report, virtually always when in weightlessness, a sensation of blood rushing to the head, heaviness of the head, as well as some hyperemia of the facial integument and sclera." We consistently observed analogous findings in antiorthostatic position, as well as some slowing of the pulse [12].

As a result of gravitational redistribution of blood and resulting neuro-humoral, somatic and vegetative reactions, depressor reflexes develop from receptors of the sinocarotid zone, Bainbridge reflex from the venae cavae, etc. This is indicative of similarity of the mechanism of parasympathetic influences in reactions of the organism to weightlessness and antiorthostatic position of the body.

The combination of antiorthostatic position and prolonged hypokinesia is of particular significance to the study of the weightlessness problem. A large team of authors [8, 17] published several papers concerning a 30-day experiment with simulation of the physiological effects of weightlessness, and they concluded that "an antiorthostatic position with a -4° tilt is a more adequate model of weightlessness than the ordinary horizontal position" [17]. A. V. Beregovkin and V. V. Kalinichenko [2], who studied reactions of the cardiovascular system in antiorthostatic position with 30-day hypokinesia, demonstrated quite moderate changes in circulatory functions. Thus, prolonged hypokinesia in an antiorthostatic position as a simulation of weightlessness with regard to hemodynamics requires further research in the aspect of reflex interaction of systems of the organism [18, 19, 26, 31]. The resilience of the organism with respect to gravitational loads is so great that with adequate conditioning there are adaptational reactions to antiorthostatic positions as well [12]. The conditioning effect of the antiorthostatic position has been confirmed by D. A. Alekseyev et al. [1]. But the position of the feet is not usually taken into consideration in the antiorthostatic position. Yet the feet are a unique reservoir which can store 500-800 ml blood, or from which the same amount can flow. And this affects systemic hemodynamics. The same is observed in the cuff test of Shval'm [35] and other methods of artificially altering blood delivery to the legs. Underestimation of the effect of foot position in antiorthostatic poses could lead to fallacious interpretation of levels of minute volume and other hemodynamic indices.

On the basis of these and other data [41], we have suggested that the antiorthostatic position be combined with elevation of the legs, which should increase the effect of simulating weightlessness. This methodological

innovation consists of the following: we used antiorthostatic positions varying in tension on a turning table, not only with the legs straight (pose No 1) but with legs flexed at 30-35° on a footrest (pose No 2). We obtained new data concerning different changes in man in this variant of postural and vegetative reactions [16, 20-22, 33, 34]. We also investigated the distinctions of kinesthesia [20], changes in skin and internal ["deep"] temperature [20], oxygenation of blood [22] and sensibility of the acoustic analyzer [23] in pose No 2.

As we see, the range of problems that are being solved by the method and theory of antiorthostatic modeling of weightlessness is widening more and more. The central problem with regard to research on the biological effects of gravitation is not so much to technically refine recording of physiological phenomena as to provide pathophysiological interpretation thereof [26, 30]. The question of using data obtained from antiorthostatic experiments for the screening of cosmonauts and development of preventive measures requires further investigation.

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BRIEF REPORTS

UDC: 612.017.1-06:629.78

HETEROPHILIC ANTIBODIES AND COMPLEMENT ACTIVITY OF RAT BLOOD SERUM AFTER FLIGHT IN KOSMOS-605 SATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 76-78

[Article by V. V. Portugalov, A. A. Ivanov and V. N. Shvets, submitted 16 Dec 74]

[Text] Prolonged stays of animals and man in a sealed space are associated with reduction [simplification] of automicroflora, and this could lead to reduction of the immunocompetent system and impairment of natural immunity [1]. Hypodynamia is another factor of space flights that lowers imunological reactivity [2]. Immunological reactions are usually mediated in the organism through humoral factors: specific (antibodies) and nonspecific (blood serum complement)[3]. The levels of heterophilic antiboides in peripheral blood (antibodies to sheep erythrocytes) are consistent with the capacity of lymphoid tissue cells to produce antibodies.

There is increased interest in complement due to expansion of conceptions about its involvement in processes of inflammation, blood clotting, immune response, etc. [4]. Determination of complement activity of blood serum offers an idea about the condition of the complement system.

The high sensitivity of both indices to the organism's response to stressors [5] was the reason for use thereof in studies of animals used in space flights.

Methods

We studied serum samples from 26 experimental and 17 control rats. We formed four groups of experimental animals: those that had spent 22 days in flight on Kosmos-605, examined on the 2d (1st group) and 27th (2d group) postflight days; the 3d and 4th groups consisted of animals kept under simulated flight conditions (with the exception of weightlessness and accelerations) for 22 days, and they were examined on the 2d and 27th days after this.

We took samples of serum from control animals and tested it on the same days as experimental animals. We evaluated the level of serum complement activity in units of 50% hemolysis (CH_{50}). Presence of agglutinin antibodies to sheep erythrocytes (0.5% erythrocyte suspension) was demonstrated in inactivated serum using the microtitrator of the Takachi system, starting with a 1/2 dilution.

Results and Discussion

On the 2d postflight day there was a significant, though statistically unreliable ($t = 1.62$), increase in blood serum complement activity (see Table). On the 27th postflight day, there was normalization of complement level. The animals in the concurrent ground-based experiment showed a similar effect on complement level.

Effects of space flight factors on complement and heterophilic antibody levels in rat blood serum

Animal group	Subgroup	Serum compl. activity, CH_{50}, ml	Hemagglutinins	
			incidence	mean intensity
1st	Animals examined on 2d postflight day Vivarium control	102,3±13,9 68,2±14,7	6/8 3/3	2+ 2+++
2d	Animals examined on 27th post flight day Vivarium control	82,3±7,2 80,4±8,5	1/6 5/5	<2 2+
3d	Animals in ground-based concurrent experiment (2d postexperiment day) Vivarium control	102,1±8,2 81,1±4,3	4/6 5/6	2+ 2+
4th	Animals in ground-based concurrent experiment (27th postexperiment day) Vivarium control	68,3±10,2 85,0±13,3	3/6 3/3	2+ 2+

Note: The number of animals with positive reaction is shown in numerator and number of animals in the group is given in the denominator.

We observed a decrease in hemagglutinin antibody content in all groups of experimental animals. We shall not discuss the statistical significance of this finding because of the small number of animals in the groups. At the same time, it should be noted, that minimum levels of antibodies are demonstrable in the recovery period in the 2d and 4th experimental groups, according to incidence of demonstration.

In our opinion, the same mechanism may be the basis for increase in serum complement activity and decrease in amount of heterophilic antibodies. Myeloid cells mature faster under the influence of the extreme space flight factors, as demonstrated morphologically [6]. In turn, this could lead to accelerated functional maturation of myeloid cells and discharge into the blood stream of one of the products they produce, i.e., complement components [4]. Probably the higher cell metabolism results in a larger amount of products of tissular decomposition that are bound in the organism by antitissular antibodies that are similar to natural hemagglutinins. The formed antigen-antibody complex binds complement, and as a result there is rapid normalization of its level in blood when the extreme factor is eliminated. We observed comparable effects previously (higher complement level and fewer antitissular antibodies) with regard to factors that are components of extreme space flight factors: hypokinesia [7] and radiation [8].

Partial reduction of the immunocompetent system with simplification of automicroflora, as a result of staying in a closed space [1], may be another cause of decrease in heterophilic antibodies. The latter, along with hypodynamia, is probably an important factor leading to lowering of heterophilic antibody level in the animals of the ground-based experiment.

We cannot derive a conclusion about the immunocompetent system of rats involved in the space flight on the basis of a single test, though it is quite informative. Our findings are indicative of the need for comprehensive examination of animals when studying their immunological reactivity.

To sum up the results submitted above, it can be stated that a 22-day stay onboard Kosmos-605 satellite led to elevation of complement level in rat blood serum and more persistent decrease in amount of heterophilic antibodies. Complement activity of blood serum was restored on the 27th postflight day, whereas the heterophilic antibody content was still low at this time.

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MEASUREMENT OF RADIATION DOSES IN THE SOYUZ-16 SPACECRAFT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1977 pp 78-79

[Article by Yu. A. Akatov, Ye. Ye. Kovalev, V. M. Petrov, M. V. Tel'tsov and V. I. Shumshurov, submitted 30 Oct 75]

[Text] The Soyuz-16 spacecraft was put into orbit with the following parameters: $H\pi$ = 177 km, $H\alpha$ = 225 km, i = 51.8°, on 2 December 1974 in accordance with the program of preparations for the joint mission of Soyuz and Apollo spacecraft. During the flight, the orbit was corrected and became close to a circular one with an altitude of ~220 km.

These orbital parameters determined the characteristics of the radiation conditions on the path and in the craft, as well as the specifications with regard to the system of monitoring them. An R-15 dosimeter was installed on Soyuz-16 to measure the integral dose of cosmic radiation; it provided the necessary information for the ground-based radiation safety service. The instrument was equipped with an ionization chamber of plexiglas that was filled with argon. During operation, the ionization current in the chamber was converted into pulses, the number of which is proportionate to accumulated dosage. The precision of dose readings in the range of 0.0125÷400 rad constitutes ±20% with dose rates of 0.005 to 100 rad/h, and ±30% with dose rates of 0.0004 to 0.005 rad/h. A record of individual exposure of cosmonauts to radiation was kept by means of a kit of thermoluminescent dosimeters that they wore at all times, and a set of nuclear photographic emulsions. The dosimeters can measure radiation doses over 50 mrad with a precision of at least 15%.

Preliminary estimates of radiation dose rates along the path of Soyuz-16 constituted a mean daily level of ~10 mrad. For the estimates, we used data on galactic cosmic radiation during the period of minimal solar activity [1] and the map of distribution of proton and electron flows at different altitudes [2]. We did not determine the effect of solar cosmic rays on radiation dose rate, since the forecast covering several days showed a very low level of solar activity and lack of bursts causing radiation hazard over the entire period of the mission.

The information from the dosimetric instrument installed in the housekeeping quarters confirmed the estimated data. Throughout the flight, the radiation dose increased uniformly and constituted 58 mrad at landing time. The doses of radiation recorded by the personal dosimeters presented wide scatter, because of nonuniformity of the radiation field in the craft, and they constituted 60-90 mrad.

These tests of the system of monitoring radiation conditions in the craft bays and levels of cosmonaut irradiation, as well as verification of the methods of estimating distribution of cosmic radiation doses along the path revealed that such a system is very effective in assuring safety of crews during manned flights in near space over analogous orbits.

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UDC: 612.115-06:612.766.2].014.47:531.15

BLOOD CLOTTING FUNCTION DURING 12-DAY IMMERSION IN WATER, AND THE PREVENTIVE ROLE OF REVOLVING ON A CENTRIFUGE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 79-81

[Article by M. A. Khudyakova and Ye. B. Shul'zhenko, submitted 22 Nov 74]

[Text] There is a sparse literature dealing with hemostasis in the presence of hypodynamia. Ye. I. Chazov and V. G. Ananchenko [11] failed to demonstrate changes in 3 out of 4 subjects during 3-day hypodynamia, while one presented increased anticoagulant and lytic properties of blood. In the case of 20-day hypodynamia, the same authors found increased fibrinolytic activity of plasma and higher blood heparin content, as well as lower heparin tolerance of plasma in the 4 subjects.

According to the report of L. M. Filatova and O. D. Anashkin [9], an increased thrombogenic potential of blood was observed on the 8th day of bedrest in horizontal position. Thereafter, a decrease in coagulating potential of blood was observed in the case of 64-day hypodynamia.

The results of Ye. I. Dorokhova [3], which were obtained with 70-day hypodynamia, revealed that there was a hypocoagulation reaction toward the end of the first 2 weeks. As the period of hypodynamia increased the hemophilic reaction also increased in all subjects.

V. A. Isabayeva and T. A. Ponomareva [4] failed to observe an increase in thrombogenic properties of blood during 10-day hypodynamia after adaptation to high altitutde. Longer periods of hypodynamia (24 days) diminished coagulant properties.

Our objective here was to study the changes in various indices of hemostasis during 12-day immersion in water and to determine whether it is possible to use increased gravitation for prevention of "decondition" of the organism during immersion.

Methods

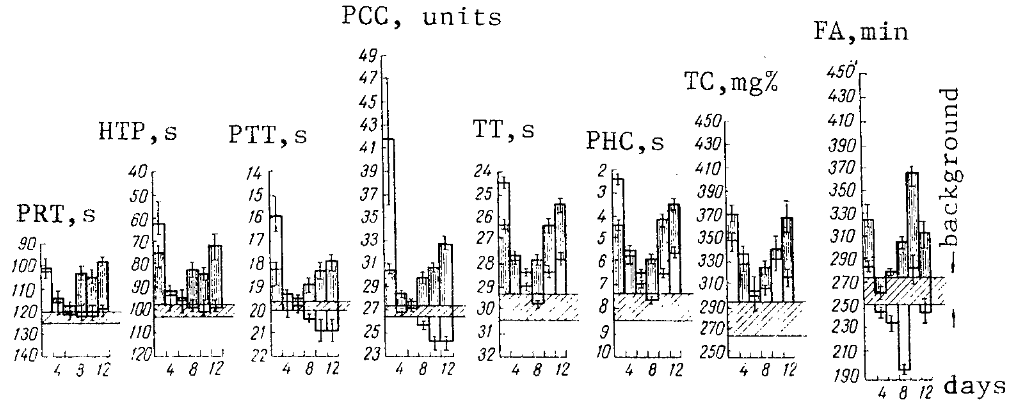
Experiments were conducted with the participation of 14 healthy men; they involved 12-day immersion in water and combination thereof with period revolving on a centrifuge. The subjects were immersed to neck level, using special waterproof fabric. The subjects were revolved on the centrifuge 1-2 times a day starting on the 7th day of immersion; they were supine on the centrifuge with the head toward the rotation axis. The acceleration generated by the centrifuge constituted 1-2 G and lasted 90-60 min. The radius of the centrifuge arm was 7.25 m. The subjects were divided into two groups: first group (six men) were submitted to "pure" immersion and the second (eight men), to immersion combined with centrifuge rotation. We collected blood samples from fasting subjects, using a silicon-coated needle, from the ulnar vein, and decanted it in silicon-coated glass test tubes. We used 0.1 M sodium oxalate solution as anticoagulant. During the test period, plasma was kept in an ice bath. To assess coagulation and anticoagulation capabilities of the organism we determined the following: plasma recalcification time (PRT) [12), heparin tolerance of plasma (HTP) [17], plasma thromboplastin time (PTT) [16], plasma thrombin time (TT) [8], prothrombin complex concentration (PCC) [16], plasma heparin content (PHC) [8], fibrin content (FC) [6] and plasma fibrinolytic activity (FA) [15]. Blood tests were made twice before immersion and during the period of immersion (2d, 4th, 6th, 8th, 10th and 12th days). The experimental data were submitted to statistical processing by the Student-Fisher method.

Results and Discussion

The Figure illustrates the changes in coagulation potential of blood of subjects in the first and second groups. It shows that in the 1st group on the 2d, 8th, 10th and 12th days, and in the 2d group, on the 2d day of immersion there was a statistically reliable decrease in PRT ($P<0.01$), PTT ($P<0.001$) and PHC ($P<0.01$), and increase in HTP ($P<0.01$), PCC ($P<0.01$), FC ($P<0.01$), and lowered FA ($P<0.02$). Both groups of subjects presented equalization of all indices on the 4th and 6th days of immersion.

Total clotting time, as well as HPT, PTT, PCC, TT, PHC, FC, were close to the initial levels in the 2d group of subjects, on the 8th, 10th and 12th days of immersion. There was an increase in FA. In the 1st group of subjects, at these same times, there was an increase in hypercoagulation due to depression of anticoagulation system function (lowering of FA and PHC, rise of HTP) and an increase in coagulation potential of blood (increase of PCCand FC).

Analysis of the obtained data is indicative of phasic changes in the system of hemostasis in man during 12-day immersion. On the 2d day there is hypercoagulation; on the 4th and 6th days the indices level off, i.e., there is an adaptation phase. Hypercoagulation increases from the 8th day on: there is significant decline of PHC, slower dissolution of fibrin clot, with increase in HTP, procoagulant concentration and FT. Preventive rotation on a centrifuge, starting on the 8th day, causes all of the indices to revert to initial levels.



Changes in indices of the blood-clotting system of man during 12-day immersion in water.

X-axis, initial background and days of immersion; y-axis, changes in indices of hemostasis, in relation to normal. White columns, changes in blood indices in 2d group of subjects; cross-hatched columns, the same for the 1st group of subjects

To sum up the findings, it can be concluded that depression of function of the anticoagulation system of hemostasis is one of the causes of hypercoagulation during immersion in water. This condition is characterized by a decrease of FA and PHC, and increase of HTP.

According to the data of different authors, the increased concentration of blood-clotting factors, which elicits an increase in thrombogenic potential in hypodynamia, may be due to diminished velocity of blood [7], thickening of blood [14, 18, 19], impaired vascular permeability [1, 2, 5]. In the presence of these states coagulation factors from formed elements and the vascular endothelium are discharged into the general blood stream.

We observed a decrease in concentration of procoagulants and increased FA following periodic rotation on the centrifuge. It is known that hypocoagulation is observed following exposure to prolonged, periodically recurrent accelerations [10]. Decreased synthesis of procoagulants by the liver is one of the causes of decreased amount of thrombus-forming proteins in blood after exposure to accelerations.

The mechanism of increasing FA after accelerations is, according to the data of Cananau [13] and other authors, related to a change in vascular permeability and discharge of tissular activator of plasminogen from the vascular endothelium into the general blood stream.

The decrease in blood procoagulants, as well as the increased FA, are beneficial factors and could prevent thrombosis during the period of immersion.

Thus, periodic rotation on the centrifuge was an effective means of preventing disturbances referable to hemostasis of the organism during immersion in water.

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DEFENSE REACTIONS OF THE ORGANISM WHILE BREATHING HIGH CONCENTRATIONS OF CARBON DIOXIDE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 81-83

[Article by O. Yu. Sidorov and Z. K. Sulimo-Samuyllo, submitted 9 Sep 74]

[Text] Man is inevitably exposed to an altered gas environment and, first of all, high concentrations of CO_2 when he is in sealed objects.

Various physiological mechanisms can be involved in protecting the organism from CO_2; however, their role and extent of participation can alter appreciably, depending on the characteristics of the hypercapnic environment. In this regard, it is of some practical interest to study the distinctions of development of defense reactions of the organism, which appear in response to the effects of gradually rising and stationary concentrations of CO_2 (to 6%).

Methods

The effects of increasing and stationary concentrations of CO_2 were studied in people.

A hypercapnic gas environment was created by adding CO_2 or CO_2+O_2 to inhaled air followed by delivery of the gas mixture through a mask in the studies involving increasing concentrations of CO_2. The concentration of CO_2 was increased to 6% in 1, 2 and 5 h, and in the experiments with stationary concentrations of CO_2 lasting 1-5 h, they constituted 2, 4 and 6%. The gas mixture was also delivered to a mask. In the long-term experiments (10 days), the subjects were kept in a special 12 m^3 chamber, in which the CO_2 content was held at the 1-2% level, oxygen content constituted 18-21%, with 50-80% relative humidity and temperature of 17-22°. Air was regenerated chemically. Twice a day, compressed air was pumped through the chamber with concurrent delivery of CO_2, which maintained the required composition of the gas environment. We recorded the subjects' pulmonary ventilation, composition of alveolar air, pulse rate, blood pressure and EKG. In addition, in the long-term experiments, we estimated reserve alkalinity of blood (RAB), erythrocyte count, hemoglobin, potassium, proteins, amino acids, as well as pH of blood.

Results and Discussion

Removal of CO_2 due to mobilization of respiratory system functions is one of the most important reactions that maintains CO_2 in the internal media of the organism on a stable level. In the experiments with progressively higher concentrations of CO_2, it was established that the presence of a certain gradient of CO_2 increment in inhaled air led to a gradual increase in pulmonary ventilation and, consequently, better elimination of excessive CO_2 from the organism. It was shown that the high rates of CO_2 increment, with which a concentration of 5.5-6% was reached in 1 h, were associated with more significant increase in pulmonary ventilation. Thus, in the studies with 1-h increase in CO_2 to 6%, pulmonary ventilation constituted 215% at the end of the experiment, in relation to the initial level. With the same concentration of CO_2, but when the increase was made over 2 h, pulmonary ventilation increased to 174%. CO_2 content of alveolar air constituted 6.5 and 6.2%, respectively, in these experiments (Table 1).

Table 1. Pulmonary ventilation and CO_2 content of alveolar air

Nature of experiment	Pulmonary ventilation, % init. level	CO_2 content of alveolar air, % ($X \pm m$)
2-h CO_2 increase to 6%	174	6,2±0,58
1-h CO_2 increase to 6%	215	6,5±0,65

Although statistical processing failed to demonstrate reliable differences in CO_2 content of alveolar air in these experiments ($P>0.05$), the substantial difference in pulmonary ventilation was definitely indicative of additional demands and more unfavorable conditions in the case of rapid increase in CO_2 in inhaled air.

In the experiments with 5-h exposure to an environment with 2% CO_2, it was shown that at first the organism prevents rise of PCO_2 in alveolar air by means of hyperventilation. Thereafter, apparently due to gradual decrease in sensitivity of regulatory mechanisms to CO_2, pulmonary ventilation decreases, and this leads to development of a hypercapnic state.

In the experiments lasting for a longer time (up to 10 days), there was even more marked deficiency of compensatory function of the respiratory system. This was manifested by lower level of pulmonary ventilation in the subjects on the last few days of the test, as compared to the first few. Thus, while ventilation constituted 11.6-12.6 liter/min on the first days, it dropped to 9.0-9.8 liter/min on the last ones.

Table 2. Change in alveolar PCO_2 and RAB when inhaled air contains 5.5% CO_2

Index	Initial background	Criterion of reliabil.	Gas environment with 5.5% CO_2, $M \pm \sigma$	Criterion of reliability
PCO_2 in alveolar air, mm Hg	$37 \pm 1,5$	$t = 2,7$ $P < 0,05$	$39 \pm 1,2$	$t = 2,7$ $P < 0,05$
RAB, vol.%	$48,8 \pm 3,0$	$t = 3.1$ $P < 0,01$	$39,5 \pm 3,8$	$t = 2,7$ $P < 0,05$

The rate of CO_2 increment in inhaled air also affected the nature of responses of the cardiovascular system. In the tests where CO_2 content was increased to 5.5-6% in 5 h, the cardiovascular system reacted in the form of slower heart rate and minor elevation of blood pressure. With increase in rate of increment (2- and 1-h increase in concentration of CO_2), instead of inhibition of cardiac activity there was excitation. Concurrently, there was greater elevation of blood pressure due to an increase in vascular tonus. A significant increase in vascular tonus, leading to lowering of pulse pressure and poorer circulation, was observed under the influence of stationary concentrations of CO_2. There were also substantial deviations in functional state of the heart (according to EKG data). In the case of slow increase in CO_2 of inhaled air, there were virtually no EKG changes in the subjects, even when a concentration of 5.5-6% CO_2 was reached. Brief exposure to stationary concentrations of CO_2 (2-4-6%) elicited extreme lability of P-P, PQ, QT intervals and increase in P and T waves. The changes in magnitude of the waves occasionally persisted in the recovery period.

In the experiments with 5-h increment of CO_2, it was shown that as long as CO_2 content of inhaled air did not exceed 3% and pulmonary ventilation was effective enough the RAB changes were insignificant and within the range of error of the test. With increase in CO_2 to 5.5%, there was an increase in PCO_2 in the alveoli and an appreciable decrease of RAB (Table 2).

In several of our experiments, a study of exchange of gases revealed that with increase in CO_2 content of the ambient atmosphere there was gradual decrease in O_2 uptake and CO_2 output. Oxygen uptake dropped from 264 ± 26 ml initially to 211 ± 22 ml/min with 3% CO_2 ($P < 0.05$) and to 176 ± 18 ml/min with 6% CO_2 ($P < 0.05$). CO_2 output constituted about 55-60% of the base level. Body temperature dropped by 0.3°.

Thus, as a result of this study, we established the distinctive features of development of defense reactions of the organism under the influence of high concentrations of carbon dioxide; they revealed that the scope, sequence and extent of involvement of different levels of compensation, as well as their effectiveness in controlling developing hypercapnia, are related to the physical parameters of CO_2 present. It was also shown that, in the case of exposure to gradually increasing concentrations of CO_2, the main protective function would be referable to the most powerful and operational mechanism,

the respiratory and cardiovascular systems. At the same time, the role of other mechanisms (buffer systems, depression of tissular metabolism, etc.) would be insignificant. The importance of additional mechanisms of compensation increases appreciably with exposure to stationary concentrations of CO_2, particularly in the case of low levels and long exposure. Furthermore, it was shown that compensatory reactions directed toward improved supply and utilization of oxygen by the organism play a certain part in the mechanism of protecting the organism from high concentrations of CO_2.

UDC: 612.398.194.014.482.4

EFFECT OF GAMMA RADIATION ON INTENSITY OF AMMONIA EXCRETION IN ALBINO RATS

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No 3, 1977 pp 83-84

[Article by K. P. Bugar', V. V. Kustov, B. I. Abidin and L. T. Poddubnaya, submitted 28 Mar 75]

[Text] Exposure of albino rats to 100 R γ-rays of radioactive ^{60}Co did not affect intensity of excretion of ammonia, while doses of 300 and 650 R diminished it.

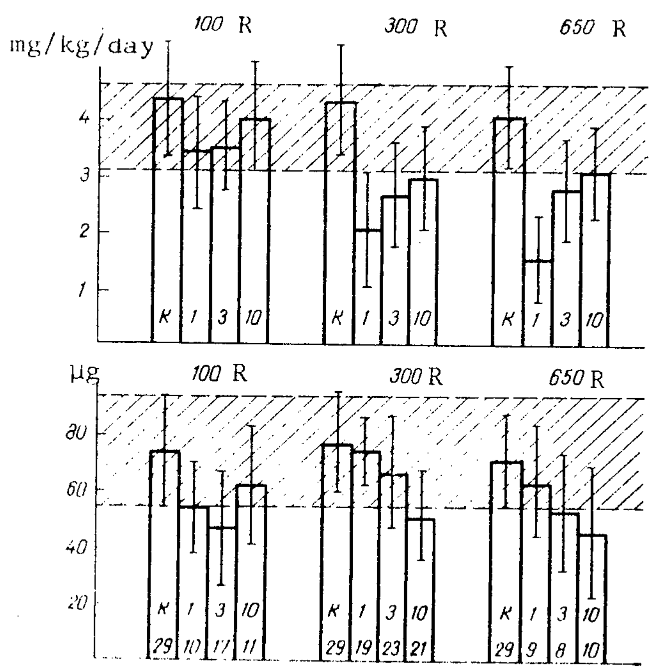
The literature concerning the effects of ionizing radiation on excretion of ammonia by irradiated animals is contradictory. According to some authors, after exposure of albino rats to 400 and 600 R x-rays there was no appreciable change in ammonia excretion in urine [1, 11]. Other researchers demonstrated an increased level thereof in urine of experimental animals (albino rats, dogs) exposed to 600 and 800 R x-rays, respectively [5, 10]. Along with these data, there is information indicating that exposure of albino rats to x-rays (700 R) leads, on the contrary, to less excretion of ammonia from the organism [3, 4]. The contradictory information could be attributed, first of all, to heterogeneity of experimental material (different species of animals, dissimilar irradiation conditions). Furthermore, in the works mentioned above, evaluation was made of the effect of radiation on ammonia excretion only according to level of excretion thereof in urine, without consideration of other routes of elimination of this product (gastrointestinal tract, lungs). At the same time, the data pertaining to overall excretion of ammonia by experimental animals could be used not only to define the mechanism of production and elimination thereof in the presence of radiation lesions, but to design life-support systems on biosatellites and formation of an artificial atmosphere. By the 18th-20th day of a mission, the ammonia level in the air of spacecraft could reach hygienically significant amounts [6].

Methods

Experiments were conducted on 12 male albino rats with initial weight of 180-220 g. The animals were divided into four groups, so that there would be the same number of animals of the same weight in each group. The

animals in the 1st, 2d and 3d groups were placed in plastic boxes and exposed to ^{60}Co γ-rays (dose rate, 27 R/min) in doses of 100, 300 and 650 R, respectively. The fourth group of animals (control) was not exposed to ionizing radiation. Some of the experimental and control rats were sacrificed on the 1st, 3d and 10th postradiation days for subsequent assay of ammonia content of blood by the method of Miller and Rice [12].

We determined elimination of ammonia by irradiated animals according to the difference between total amount of this product in condensate and air of the chamber after experimental and control rats had spent 24 h in it (each group consisted of 10 animals and the tests were repeated 3-4 times). Oxygen and carbon dioxide content of the artificial atmosphere in the hermetically sealed chamber, 93 liters in size, was kept at 20-24 and 0.2-1%, respectively. A constant air temperature (20°) and relative humidity (not exceeding 70%) were maintained by means of a system of thermoregulation and collection of condensate of atmospheric moisture. Ammonia content in the air of the chamber and condensate was determined by the method of M. I. Poletayev and N. A. Andreyeva [7].



Effect of γ-radiation on blood ammonia content and intensity of excretion thereof.
Striped band, physiological "norm" of index; K, initial level thereof. The numbers in the columns refer to day of observation on top and number of animals on the bottom.

Results and Discussion

The Figure illustrates the results of our experiments. Exposure of the animals to ^{60}Co γ-rays in a dosage of 100 R (1st group) did not have an appreciable effect on ammonia level in blood and total elimination thereof. With increase in radiation dose to 400 R (2d group) and 650 R (3d group), blood ammonia content diminished in experimental animals. However, a substantial difference between base value of this index, as well as the physiological ammonia "norm" in rat blood and amount of this product in the blood of experimental animals was recorded only on the 10th postradiation day. The intensity of excretion of ammonia also diminished: on the 1st and 3d postradiation days, with exposure to doses of 300 and 650 R, daily excretion of ammonia per kg body weight differed appreciably from the initial level of this index in experimental rats, and it was considerably lower than the physiological range in control animals. By the 10th experimental day, the intensity of excretion of ammonia in irradiated rats virtually reached the lower range of the physiological norm.

Thus, the results of our experiments revealed that γ-radiation has no effect on excretion of ammonia by irradiated animals with a dosage of 100 R, whereas in doses of 300 R and 650 R it lowers excretion thereof. The lower intensity of elimination of this product after exposure to 300 and 650 R ionizing radiation could be due, to some extent, to impaired functional state of the gastrointestinal tract, which is the main supplier of ammonia in the organism [2] and decreased excretion thereof in urine due to inhibition of the process of deamination of amino acids [8] and biogenous amines [1], which is one of the sources of ammonia formation in the organism. Evidently there are also other mechanisms involved in this phenomenon, and they require special investigation.

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OTOLITH SYSTEM FUNCTION IN COSMONAUTS FOLLOWING SPACE MISSIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1977 pp 85-86

[Article by F. A. Solodovnik, submitted 7 Jul 75]

[Text] The experience of flying in space indicates that some cosmonauts present symptoms of motion sickness and illusions of spatial position on the 1st day of missions. It is believed that such disorders are the result of distinctive stimulation, in an environment that is unusual to man, of receptors of physiological systems that control spatial position and mainly the vestibular analyzer [1, 2, 5, 6].

Perhaps prolonged weightlessness leads to functional reorganization of the otholithic system, and after returning to earth the cosmonauts have to undergo reverse adaptation to gravitation conditions.

The objective of this work was to investigate the functions of the otolith system of cosmonauts before and after a space mission.

Methods

These studies were pursued using a swing suspended on four rods, with revolving seat [3]. The back and seat of the swing were lined with porolon. The cosmonaut was strapped tightly in the swing seat. His head was tiled 30° forward, the eyes were shut and light-proof glasses were worn. The magnitude of deviation of the swing from the vertical line was recorded on a special scale. In order to disorient the cosmonaut, he was rotated in the swing chair prior to the study, at the rate of 15°/s. After 2-3 turns, the seat was stopped in one of six positions: 0 and 180° by swinging forward and backward; 90 and 270° positions to the left and right, and 225 and 315° at an angle of 45°. To rule out the possibility of orientation in relation to the direction of swing movement, the studies involved stopping the swing in the following positions: 90, 225, 0, 315, 270 and 180°.

After rotating the cosmonaut in the swing seat, 20 s after disappearance of the illusion of reverse rotation, we began to push the swing, gradually increasing amplitude to 0.5 cm. Two complete swinging movements were made (two periods) at this amplitude; the amplitude was then increased by 0.5 cm and another two swings were performed, etc. With increase in amplitude, the

cosmonaut fixed the time of appearance of the sensation of swinging and, if he was able, indicated the direction of movement of the swing with the palm of his hand. But if he could not determine the direction of swinging at the start, i.e., at a low amplitude, we continued to increase the amplitude of swinging until he was able to confidently and correctly determine his position in relation to the direction of movement.

Maximum acceleration in the horizontal plane was calculated using the following formula:

$$a = \frac{A}{l} g$$

where a is linear acceleration, A is amplitude of swinging, l is the length of the swing rods and g is acceleration of free-falling body.

We tested functions of the otolith system of the cosmonauts before a mission and 3 days after landing. A total of 10 cosmonauts participated in our studies; they had performed space missions lasting 3 to 28 days.

Results and Discussion

All of the cosmonauts perceived rather accurately the start of swinging under the influence of low linear accelerations, and they determined the direction of movement of the swing mainly after subsequent increases in swinging amplitude. A comparison of the results of testing threshold levels of linear accelerations before and after space flights failed to demonstrate appreciable differences (see Table). Nor were there any reliable changes in threshold levels of perception of the vector of linear acceleration, regardless of the cosmonaut's position in relation to direction of movement of the swing. The minor drop of all mean indices after a space flight was perhaps related to a somewhat higher emotional state of the cosmonauts at this time.

Threshold levels of perception of linear acceleration by cosmonauts, cm/s^2 (M±m)

Time of examination	Threshold of perception of linear acceleration	Threshold of perception of direction of linear acceleration. Cosmonaut's position in relation to direction of movement of swing		
		head in direct.of movement	90° angle	45° angle
Before flight	4.0±0.24	10.7±1.08	11.8±0.56	17.6±1.71
After flight	3.2±0.43	7.0±1.03	8.5±1.95	17.2±1.45

When swinging, mainly periodically changing direction and magnitude of linear acceleration affect receptor systems of the organism, as well as minimal stimuli of no practical significance: change in force of gravity and centripetal acceleration. It is known that the receptors of the otolith system are stimulated with tangential displacement of otoliths [7, 8].

Swinging at a low amplitude stimulates primarily the otolithic system in man. This has been convincingly demonstrated in the experiments of Walsh [9].

The obtained results of studies of threshold levels of perception of linear acceleration and vector thereof do not differ appreciably from the results of experiments involving people of other than flight specialties [4].

A comparison of the results obtained on cosmonauts who had been on space missions varying in duration also failed to demonstrate differences in capacity to perceive linear acceleration.

Thus, no appreciable deviations of otolith system functions were demonstrated in cosmonauts 3 days after they had been on space missions lasting 3 to 28 days. The obtained data are consistent with clinical observations, which failed to demonstrate any deviations in vestibular function. Perhaps, with up to 28 days of weightlessness the otolithic system remains unchanged, or else the deviations that do appear in its function are brief and soon disappear upon returning to earth's gravitation. This question requires further investigation.

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SUDDEN LOSS OF CONSCIOUSNESS IN PILOTS WITH LOW INTRAOCULAR PRESSURE DURING EXPOSURE TO G FORCES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 86-87

[Article by Yu. Domashuk and M. Voytkovyak, submitted 14 Dec 74]

[Text] In the pilot profession, sudden loss of consciousness is particularly dangerous. Various factors can be the causes of this phenomenon: hypoxia, hyperventilation, G forces and others [2, 3, 5]. Among them, "head-pelvis" G forces are rather significant.

It should be noted that loss of consciousness in the presence of G forces is not usually sudden, and it is virtually always preceded by visual disturbances in the form of a gray or black covering [1, 4].

During linear increment of G forces at the rate of 0.1 units/s, marked impairment of peripheral vision should occur 8-12 s (or 0.8-1.2 units) prior to loss of consciousness. However, mass screening of pilots on a centrifuge (determination of range of endurance with intact vision with linear increment of G forces) revealed instances when loss of consciousness was not preced by disturbances referable to vision. The present study was conducted in order to determine the causes of this phenomenon.

Methods

We studied two groups of pilots; the first group consisted of seven people. These subjects developed sudden loss of consciousness without visual precursors in a test of G force endurance in experiments on a centrifuge. The second (control) group consists of 15 pilots, in whom the range of endurance was determined on the basis of visual disorders. All of the subjects had undergone a comprehensive clinical and laboratory work-up prior to the experiments, and the results failed to demonstrate any deviations from normal.

We measured intraocular pressure with a Schioetza tonometer immediately after exposure to G forces. Intraocular pressure was also measured before the experiment in the second group of pilots. In addition, we checked pulse rate and arterial pressure both before and after the experiment.

We were particularly concerned with comparative determination of intraocular pressure in both groups of pilots, as well as the effects of G forces on this index.

Results and Discussion

The range of endurance of G forces constituted 4.5 to 7.4 units (mean of 6.29±0.962 units) in the first group of pilots, and there was no statistically reliable difference from the second group (6.50±0.915 units), in which maximum endurance was evaluated on the basis of visual disturbances. Moreover, circulatory indices (pulse and arterial pressure) were similar in both groups of subjects.

However, intraocular pressure, measured after the experiment, was below the physiological norm in the first group, constituting 11.70±1.44 mm Hg, which was reliably different from the same index in the second group (16.27±3.01 mm Hg).

The results of studying the effects of maximum tolerable G forces on intraocular pressure revealed a statistically reliable ($P<0.01$) drop of intraocular pressure (from 18.79±2.90 in the background to 16.27±3.01).

Thus, as indicated by the data obtained, low intraocular pressure during exposure to G forces may be the cause. [sic]

On the basis of the results of our investigation and in view of the fact that we failed to observe instances of sudden loss of consciousness in individuals with normal intraocular pressure, it can be concluded that one should measure intraocular pressure in all pilots exposed to G forces, for preventive purposes.

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NEW BOOK DEALS WITH PHYSIOLOGICAL FUNCTIONS OF THE VESTIBULAR SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 pp 87-88

[Review by M. D. Yemel'yanov of the book "Fiziologicheskiye Funktsii Vestibulyarnoy Sistemy" by A. Ye. Kurashvili and V. I. Babiyak, Izdatel'stvo Meditsina, Leningrad Department, 1975, 279 pages]

[Text] The authors' objective was to summarize the information in the literature and report the results of their own clinicophysiological research on pressing problems of physiology of the vestibular analyzer.

The book consists of an introduction, seven chapters, conclusion and bibliography.

Chapter 1 describes the structure of the peripheral part of the vestibular analyzer (receptors) and vestibular nuclei. Their efferent (outgoing) and afferent (incoming) relations are traced to some elements of the central nervous system, and their functional characteristics are given.

The chapter is, to some extent, a repetition of material summarized in the monographs of Sentagotay (1950-1952), Brodal et al. (1966), A. N. Razumeyev and A. A. Shipov (1969) and Ya. A. Vinnikov (1971). However, it is apparently necessary, since it offers an integral idea about the objectives of the book.

The authors could be reproached for failing to provide a clearcut structural and functional definition of the very concept of vestibular analyzer.

Chapter 2 discusses the concept of an adequate vestibular stimulus in the form of mechanical forces. Acceleration and velocity cannot be stimuli on their own, i.e., carriers of energy. It would seem that such an interpretation precludes use of the term "acceleration" as a stimulus of vestibular receptors. Yet many researchers disregard this fine point in their work.

The mechanisms of excitation in the semicircular canals and otolith system are described rather well, with mathematical computations covering the intensity and duration of a stimulus, as well as its vector.

Cupulometry is submitted to critical discussion. Load tests and continuous stimulation of the vestibular system using measured, variable-polarity accelerations are considered to be more promising methods for evaluating vestibular function.

Unfortunately, not enough attention is given to a discussion of inadequate methods of vestibular stimulation.

Chapters 3 and 6 cover the general pathogenetic mechanisms of the processes in question. Perhaps it would have been more expedient to do this in one chapter. There is graphic demonstration of the fact that it is important to hold spatial coordinates that are fixed in relation to the gravitational vertical in the field of vision to retain equilibrium of the body. In this regard, a section on vestibular nystagmus occupies a significant place.

Chapter 6 deals with the important question of interaction of vestibular and visual analyzers. There is discussion of vestibular influences on fixing function of the eyes and some distinctions of tracking movements. Modulation of efferent fixation function is, in the authors' opinion, the result of central convergence of vestibular and optokinetic afferents (reticular formation, thalamus, cerebral cortex) and formation of a modified spatial image on the basis thereof. For this reason, a "jump" or turn of the eyes in a specified direction is very precise (even in the absence of a visible target).

Chapter 4 is of interest to physiologists. There is valid substantiation of the borderline between normal vestibulovegetative and pathological reactions. The former supply the energy balance of the muscle system in maintaining a pose, equilibrium and spatial orientation, i.e., in the presence of functional vestibulosomatic reflexes. In this sense, the capacity to activate adaptational and trophic function of the autonomic nervous system is attributed to the vestibular analyzer. The authors' own experiments enabled them to expound the hypothesis that there is afferent representation of the vestibular analyzer in elements of the limbic system.

Efforts to find features in common in motion sickness and Selye's syndrome lead to some contradictions. The fact that some individuals are affected by motion sickness and others are not, discrete forms of these processes, lack of pattern in development of vegetative disorders and the classical triad of Selye in virtually all cases are not consistent with the Selye syndrome.

The authors discuss the hypothalamus as the main source of the first and second phases (in their classification) of the adaptation reaction in motion [sea] sickness and transformation of a nervous signal into a humoral one.

The statement that an angioneurotic component is the initial pathogenetic mechanism of the entire set of symptoms of sea sickness (p 160) is debatable.

At the same time, in our opinion, studies directed toward determination of the functional state of carotid glomeruli and their role in regulating

circulation in the presence of vestibular stimulation are not without interest. Data have been obtained on a different level of regulation in the presence of specific vestibular stimuli and the effects of stimulation of the carotid sinus on nystagmus.

Chapter 5 deals with little-studied aspects of vestibulology. The authors develop the teaching on the essence of excitation in nerve centers. It is stressed that processes arising in the vestibular system with simulation of successive reactions do not end with their primary manifestation, but continue in the form of phasic reactions. The number of phases and their duration depend on the force of the vestibular stimulus.

In Chapter 7, the authors raise very validly the question of involvement of the set of analyzers in evaluation of spatial position, on the one hand; they attribute appropriate significance to psychophysiological aspects. On the other hand, they exaggerate somewhat the role of the vestibular system.

We tend to consider interaction between the visual and vestibular analyzers from the standpoint of more refined correlations occurring as a result of the effects of various stimuli, both on the level of vestibulooculomotor reactions and cortical sensory relations.

In the conclusion, concrete routes of future research are delineated with reference to functions of the vestibular system, of which the following are the most important in our opinion: the problem of analyzer interaction on different levels of nerve structures, mechanisms of sea sickness, spatial illusions and control of vestibular reflexes.

On the whole, the book merits a high rating.

This monograph will be of definite interest and usefulness to a wide circle of readers: otorhinolaryngologists, physiologists, mainly in the field of space physiology, psychologists, etc.

UDC: 613.693(092)Volynkin

BIOGRAPHY OF YUVENALIY MIKHAYLOVICH VOLYNKIN (ON HIS 70TH BIRTHDAY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1977 p 89

[Article by the editorial board]

[Text] There are people whose life has many directions and wide scope; their endeavors are particularly remarkable, and their personal charm compels all those around them to treat them with the deepest respect. Yuvenaliy Mikhaylovich Volynkin, a brilliant specialist, excellent organizer, ardent patriot and remarkable human being, is unquestionably such a person.

Yu. M. Volynkin graduated from the Military Medical Academy imeni S. M. Kirov in 1932.

Yuvenaliy Mikhaylovich first came into aviation medicine as a medical laboratory technician, then as head of the psychophysiological laboratory.

In 1936, Yuvenaliy Mikhaylovich was promoted to the post of senior inspector for medical support of high-altitude and high-speed flights, where his great organizational talents were manifested.

In 1939, Yu. M. Volynkin participated in the Soviet-Finnish War, as head of an evacuation hospital. He was an active participant in creating the hospital base of the Eighth Army. This was the birth of a great organizer.

The Great Patriotic War found Yuvenaliy Mikhaylovich as one of the heads of the Main Military Medical Administration of the Soviet Army. Yuvenaliy Mikhaylovich developed and created new and original structures of the medical service of the combat units of the USSR Armed Forces. He was directly involved in implementing formation of a network of front-line hospital bases and deployment of a network of educational medical institutions. Training of qualified medical personnel for the Armed Forces was implemented under the direct supervision of Yu. M. Volynkin. In 1951, Yuvenaliy Mikhaylovich was assigned deputy head of the Military Medical Academy imeni S. M. Kirov, where he implemented major organizational and methodological measures directed toward reorganizing the training of military physicians, with due consideration of the knowhow gained in the Great Patriotic War of 1941-1945.

From 1954 to 1968, Yu. M. Volynkin implemented a number of brilliant organizational measures; he displayed a profoundly creative approach to planning and performance of difficult scientific work in the field of aviation and space research.

During this period, screening and training of the first cosmonauts were implemented under his immediate supervision; the principles of medical and medico-technical support of space flights in our country were substantiated at this time.

In 1969, Yuvenaliy Mikhaylovich was transferred to the reserves with the rank of Lt General. Since then and to the present time, as assistant to the director of the Institute of Biomedical Problems, USSR Ministry of Health, Yu. M. Volynkin is successfully solving all of the organizational-methodological and planning problems pertaining to scientific research at this institute.

We are particularly proud to have had the opportunity to be with this charming man, wise organizer and expert with enormous experience. The government has shown its appreciation to Yuvenaliy Mikhaylovich Volynkin for his brilliant handling of large and responsible State assignments, his exceptional industriousness and high degree of versatile qualifications; he is the recipient of two Orders of Lenin, orders of the Red Banner and Red Banner of Labor, three orders of the Red Star and many medals.

Along with his numerous disciples and comrades in arms, we sincerely wish Yuvenaliy Mikhaylovich Volynkin good health and new creative achievements for the good of our Great Homeland.

UDC: 629.78(092)Korolev

OBITUARY OF SERGEY PAVLOVICH KOROLEV (ON HIS 70TH BIRTHDAY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1977 p 90

[Article by the editorial board]

[Text] An era of significant achievements is linked with the name of Academician Sergey Pavlovich Korolev, oustanding Soviet scientist, designer of space rocket systems, twice named Hero of Socialist Labor and one of the founders of practical cosmonautics: development of high-power space rocket systems, the first flight in space of Yu. A. Gagarin, extravehicular activity of man in space, photography of the moon, creation of interplanetary stations to the moon, Venus and Mars. In each of these achievements, there was wide use of the scientific and technical ideas of S. P. Korolev; to each of them he made an appreciable contribution, thanks to his outstanding organizational skills and talents of a great scientist, who was able to provide, for a number of years, the directions for development of Soviet cosmonautics and to guide the work of many scientific research and designing teams to perform their assigned tasks.

S. P. Korolev always paid much attention to problems of biomedical support of manned space missions; he constantly collaborated in the creation and development of a new branch of science, space biology and medicine.

Even in the early days of his scientific activities, in 1934, he wrote in his work "Rocket Flight Into the Stratosphere": "Let us discuss the characteristics of jet craft equipped with engines using liquid fuel. First, there is the crew.... Second, life support.

This will include all the devices, instruments and equipment to maintain living conditions for the crew and efficiency at high altitudes." And in his subsequent work, Sergey Pavlovich repeatedly returned to this problem, devoting his attention mainly to development and safe and reliable life support devices in space.

S. P. Korolov attributed special importance to question of screening and training cosmonauts. He was a frequent visitor at Zvezdnyy town; he constantly observed the studies of future cosmonauts; he delivered lectures

to them himself and was a strict interrogator at their examinations. Sergey Pavlovich collaborated successfully and maintained personal contact with outstanding scientists and organizers of Soviet medicine: A. I. Burnazyan, V. A. Engel'gardt, N. M. Sisakyan, V. V. Parin, A. V. Lebedinskiy, Yu. M. Volynkin, V. I. Yazdovskiy and other figures in Soviet science.

Many of the scientific ideas and technical proposals of S. P. Korolev were implemented after his death. The long-term orbital stations, spacecraft for exploration of Venus, systems of radio communication in space and specialized satellites of significance to the national economy are the next landmarks of Soviet cosmonautics, in each of which there is a particle of selfless labor and talent of Sergey Pavlovich Korolev.

S. P. Korolev wrote: "I cannot help wanting to exclaim how much has been done and accomplished, and at the same time cannot fail to state how little has been accomplished, how much more there is still to do."

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